STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 182692

TO: Marcela Cordero Garcia **Location: REM/3A30/3C18** **Art Unit: 1654** **March 22, 2006** **Case Serial Number: 10/802013**	**From: P. Sheppard** **Location: Remsen Building** **Phone: (571) 272-2529** **sheppard@uspto.gov**

Search Notes

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=> d his ful

     FILE 'REGISTRY' ENTERED AT 12:21:18 ON 22 MAR 2006
L1                STR
L2                STR
L3           1666 SEA SSS FUL L1 OR L2
L8                STR
L22               STR
L23             2 SEA SUB=L3 SSS FUL L8 AND L22

     FILE 'HCAPLUS' ENTERED AT 12:45:18 ON 22 MAR 2006
L27             6 SEA ABB=ON  PLU=ON  L23
                  D STAT QUE
                  D IBIB ABS HITSTR L27 1-6

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L44             6 SEA ABB=ON  PLU=ON  L43 NOT (L27 OR L33)
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                  D IBIB ABS HITSTR L44 1-6
L45            49 SEA ABB=ON  PLU=ON  "MOLINO B"/AU OR "MOLINO B F"/AU OR
                  ("MOLINO BRUCE"/AU OR "MOLINO BRUCE F"/AU OR "MOLINO BRUCE
                  FRANCIS"/AU)
L46            21 SEA ABB=ON  PLU=ON  ("HAYDAR S"/AU OR "HAYDAR S N"/AU) OR
                  "HAYDAR SIMON"/AU OR "HAYDAR SIMON N"/AU
L47             9 SEA ABB=ON  PLU=ON  ("HEMENWAY MICHAEL S"/AU OR "HEMENWAY
                  MICHAEL SCOTT"/AU)
L49            76 SEA ABB=ON  PLU=ON  L45 OR L46 OR L47
L50           563 SEA ABB=ON  PLU=ON  "YANG Z"/AU OR YANG ZHICAI?/AU
L51           105 SEA ABB=ON  PLU=ON  "RICH JOSEPH"/AU OR ("RICH JOSEPH O"/AU OR
                  "RICH JOSEPH OSWALD"/AU) OR RICH J/AU OR RICH J O/AU
L52             1 SEA ABB=ON  PLU=ON  L50 AND L51
L54         22554 SEA ABB=ON  PLU=ON  L3 OR ?CYCLOSPOR?
L55             5 SEA ABB=ON  PLU=ON  (L50 OR L51) AND L54
L56            77 SEA ABB=ON  PLU=ON  (L49 OR L52 OR L55) NOT (L33 OR L27)
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                  D IBIB ABS L56 1-77

     FILE 'REGISTRY' ENTERED AT 13:12:01 ON 22 MAR 2006
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FILE HOME

FILE REGISTRY
Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 21 MAR 2006 HIGHEST RN 877591-95-2
DICTIONARY FILE UPDATES: 21 MAR 2006 HIGHEST RN 877591-95-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE HCAPLUS

FILE COVERS 1907 - 22 Mar 2006 VOL 144 ISS 13
FILE LAST UPDATED: 21 Mar 2006 (20060321/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>

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=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 12:45:18 ON 22 MAR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 22 Mar 2006  VOL 144 ISS 13
FILE LAST UPDATED: 21 Mar 2006  (20060321/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=>
=>

=> d stat que
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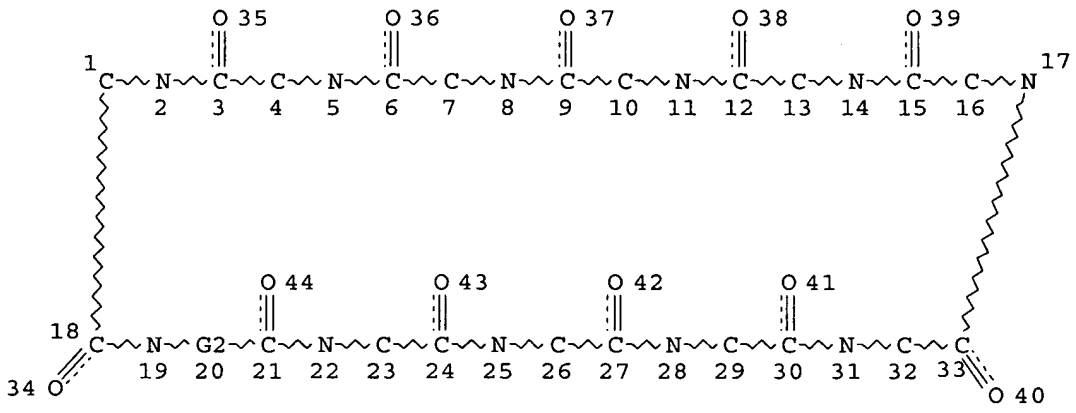


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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  49
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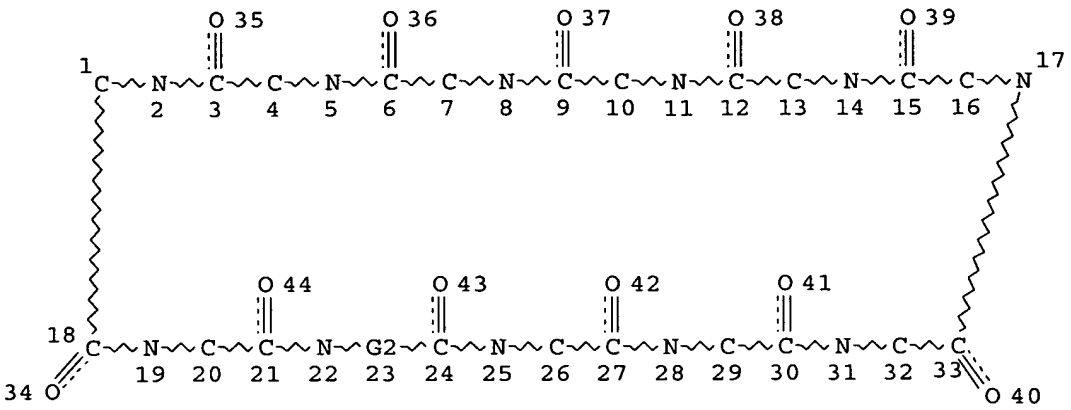

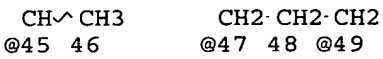

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 49

STEREO ATTRIBUTES: NONE
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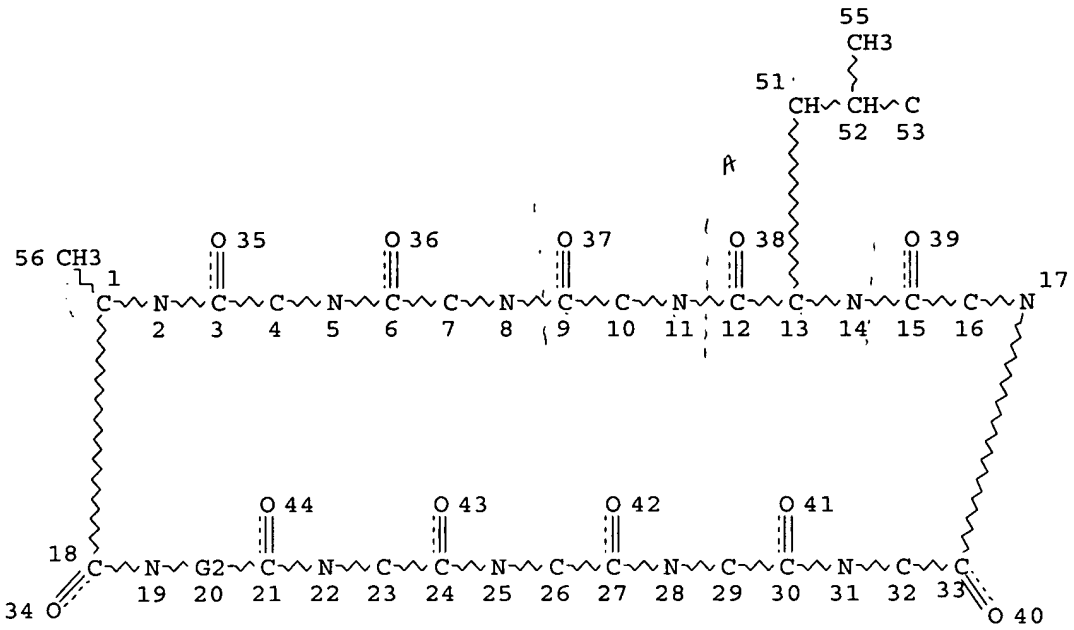
L8 STR



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@45 46 @47 48 @49

VAR G2=45/47-19 49-21
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DEFAULT MLEVEL IS ATOM
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GRAPH ATTRIBUTES:
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STEREO ATTRIBUTES: NONE
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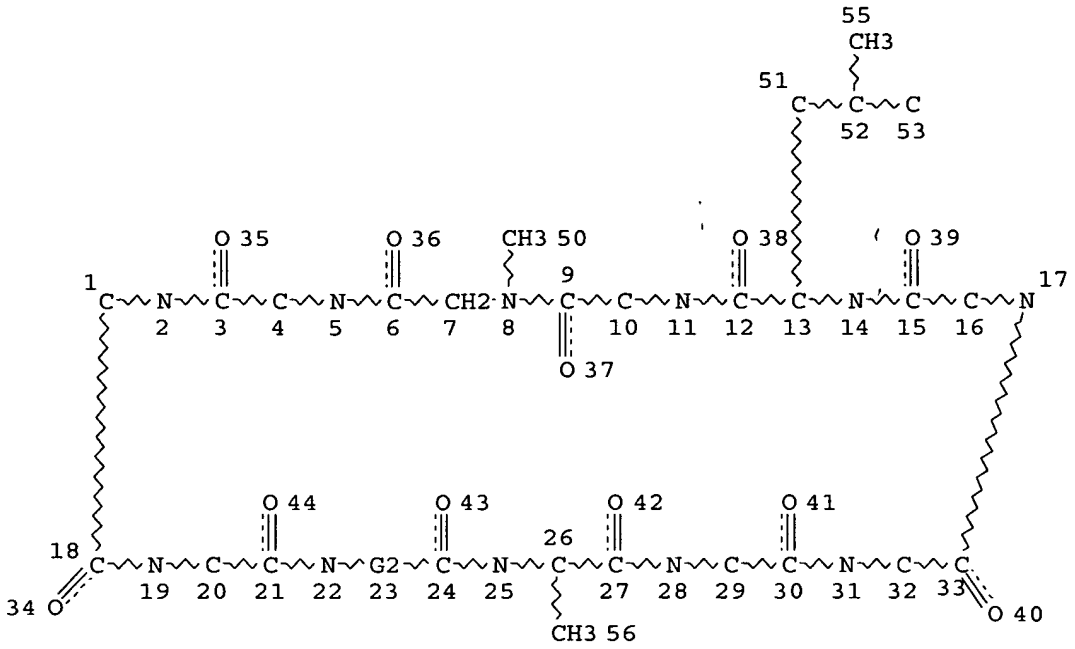
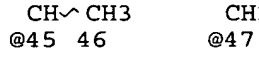




VAR G2=45/47-22 49-24
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 55

STEREO ATTRIBUTES: NONE
L23 2 SEA FILE=REGISTRY SUB=L3 SSS FUL L8 AND L22
L27 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L23

=>
=>

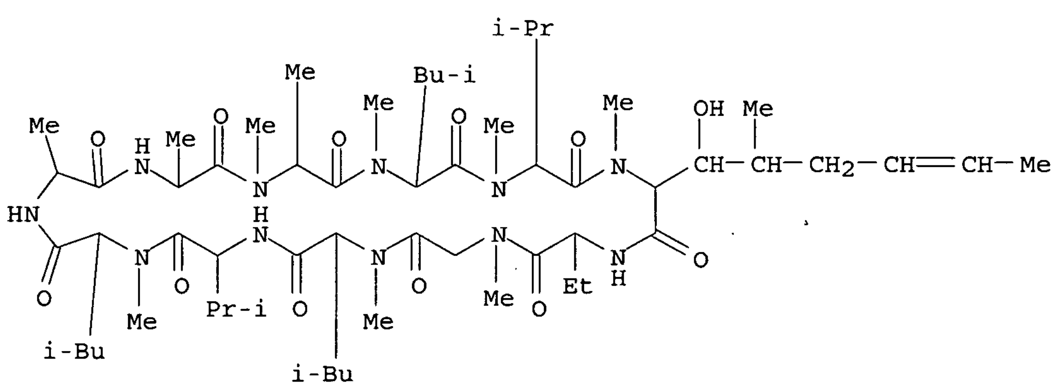
=> d ibib abs hitstr l27 1-6

L27 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:475261 HCAPLUS
DOCUMENT NUMBER: 121:75261
TITLE: Human Cyclophilin C: Primary Structure, Tissue Distribution, and Determination of Binding Specificity for Cyclosporins
AUTHOR(S): Schneider, Helmut; Charara, Nadine; Schmitz, Rita; Wehrli, Susi; Mikol, Vincent; Zurini, Mauro G. M.; Quesniaux, Valerie F. J.; Movva, N. Rao
CORPORATE SOURCE: Sandoz Pharma Ltd., Basel, CH-4002, Switz.

SOURCE: Biochemistry (1994), 33(27), 8218-24
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A cDNA for human cyclophilin C (Cyp-C) was isolated from a human kidney cDNA library. Northern blot expts. with several human tissues and cell lines revealed that Cyp-C is less abundant than Cyp-A. The amount of Cyp-C mRNA was 10-fold lower than that of Cyp-A in kidney. Expression of human Cyp-C in the kidney is not significantly elevated compared to pancreas, skeletal muscle, heart, lung, and liver. This argues against a previously postulated specific role for Cyp-C in the nephrotoxic effects of CsA in humans, based on the studies of its relative abundance in murine kidney. It is present in extremely low concns. in brain and in the Jurkat T cell line. The binding of recombinant human Cyp-A, -B, and -C to cyclosporin A (CsA) was studied by immunochem. methods. The relative affinity of Cyp-C for CsA is lower by a factor of 2 than that of Cyp-A, which itself is 10-fold lower than that of Cyp-B. Cross-reactivity studies with a series of Cs derivs. showed that Cyp-C binds CsA with a fine specificity similar to that of Cyp-A and Cyp-B. Cs amino acid residues 1, 2, 10, and 11 seemed essential for the interaction with all three Cyp subtypes. However, Cyp-C tolerates a greater variety of structures on Cs position 2 than Cyp-A does, suggesting that this residue of CsA might not be in tight contact with Cyp-C. This was confirmed by modeling of human Cyp-C on the structure of the complex formed by Cyp-A and CsA. The knowledge of the fine specificity of human Cyps for CsA and of their expression levels may provide better insights into how CsA acts on its different target proteins in vivo.

IT **112067-18-2**
RL: BIOL (Biological study)
(cyclophilin C and A and B binding specificity for, of human)
RN 112067-18-2 HCAPLUS
CN Cyclosporin A, 3-(N-methyl-L-alanine)- (9CI) (CA INDEX NAME)



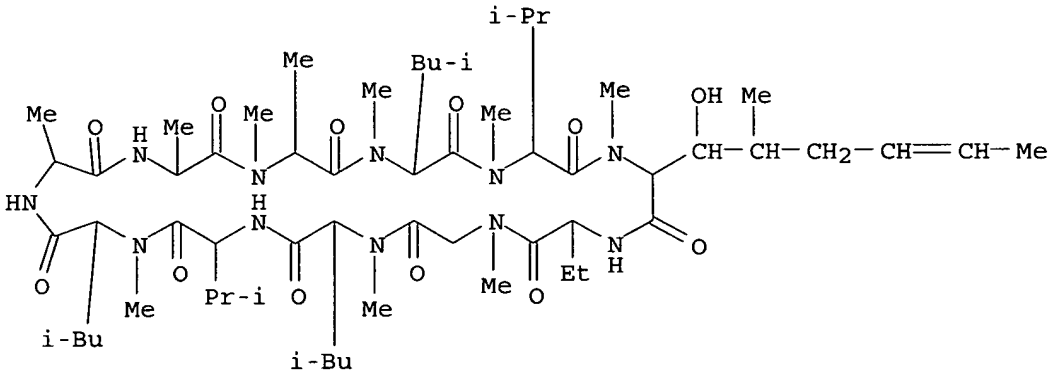
L27 ANSWER 2 OF 6 HCAPLUS
ACCESSION NUMBER: 1991:199063 HCAPLUS
DOCUMENT NUMBER: 114:199063
TITLE: Is cyclophilin involved in the immunosuppressive and nephrotoxic mechanism of action of cyclosporin A?
AUTHOR(S): Sigal, Nolan H.; Dumont, Francis; Durette, Philippe; Siekierka, John J.; Peterson, Laurence; Rich, Daniel H.; Dunlap, Brian E.; Staruch, Marie J.; Melino, Michael R.; et al.
CORPORATE SOURCE: Dep. Immunol. Res., Merck, Sharp and Dohme Res. Lab.,

Rahway, NJ, 07065, USA
SOURCE: Journal of Experimental Medicine (1991), 173(3), 619-28
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The major cytosolic protein for cyclosporin A (CsA), cyclophilin, may be directly involved in mediating the immunosuppressive activity of this drug. Inhibition of the related peptidyl-prolyl cis-trans isomerase (PPIase) may inhibit murine T-cell activation. The nephrotoxicity observed with CsA may also be related to inhibition of PPIase-dependent pathways in cells other than lymphocytes. Using a series of 61 cyclosporin analogs, a good correlation was found between cyclophilin binding and immunosuppressive activity for most analogs. A number of compds. of distinct structural classes interact with cyclophilin, but were much less immunosuppressive than expected. The inability of these analogs to inhibit lymphocyte activation could not be explained by their failure to enter the cell and bind to cyclophilin under the conditions used in the cellular assays. The nonimmunosuppressive analog MeAla-6, which bound well to cyclophilin and was active as a PPIase inhibitor, did not induce any renal pathol. in vivo. The analog MeBm2t, which was immunosuppressive in vitro, possessed little or no activity as a PPIase inhibitor. These findings pose serious questions concerning the role of cyclophilin in mediating CsA immunosuppressive and nephrotoxic activities. They raise doubts about whether PPIase has a direct function in lymphocyte signal transduction.

IT **112067-18-2**
RL: PRP (Properties)
(immunosuppressant and nephrotoxic effects of, cyclophilin binding and structure in relation to)

RN 112067-18-2 HCAPLUS
CN Cyclosporin A, 3-(N-methyl-L-alanine)- (9CI) (CA INDEX NAME)



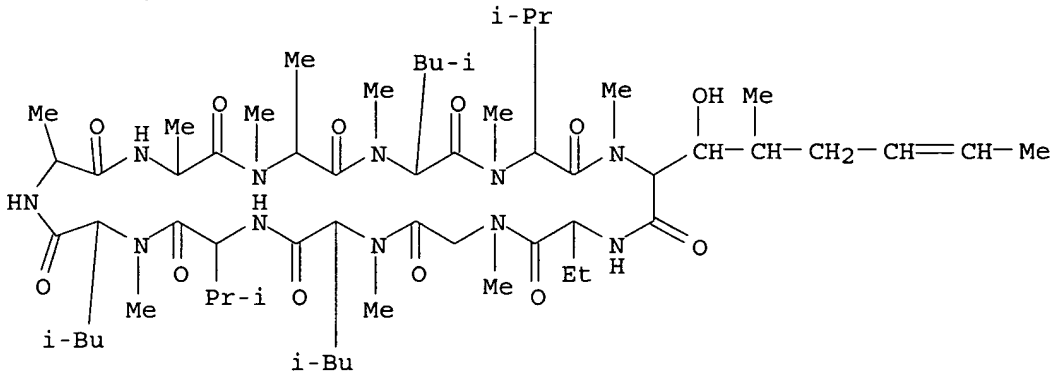
L27 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:542019 HCAPLUS
DOCUMENT NUMBER: 109:142019
TITLE: A study of the correlation between cyclophilin binding and in vitro immunosuppressive activity of cyclosporin A and analogs
AUTHOR(S): Durette, P. L.; Boger, J.; Dumont, F.; Firestone, R.; Frankshun, R. A.; Koprak, S. L.; Lin, C. S.; Melino, M. R.; Pessolano, A. A.; et al.
CORPORATE SOURCE: Dep. Immunol., Merck Sharp and Dohme Res. Lab.,

Rahway, NJ, USA
SOURCE: Transplantation Proceedings (1988), 20(2, Suppl. 2), 51-7
CODEN: TRPPA8; ISSN: 0041-1345
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To establish whether cyclophilin (CyP) is the pharmacol. relevant cyclosporine A (CsA) receptor, the CyP binding vs. immunosuppressive activity was measured for an extensive, structurally varied group of CsA analogs. Overall, CyP binding paralleled immunosuppressive activity. Other than MeAla6-CsA, the few exceptions to the correlation could be ascribed to cellular metabolism These results strongly implicate CyP or a related protein in the mechanism of action of cyclosporin.

IT **112067-18-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and cyclophilin binding and immunosuppressive activity of)

RN 112067-18-2 HCAPLUS
CN Cyclosporin A, 3-(N-methyl-L-alanine)- (9CI) (CA INDEX NAME)



L27 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:143029 HCAPLUS
DOCUMENT NUMBER: 108:143029
TITLE: Cyclophilin binds to the region of cyclosporine involved in its immunosuppressive activity
AUTHOR(S): Quesniaux, Valerie F. J.; Schreier, Max H.; Wenger, Roland M.; Hiestand, Peter C.; Harding, Matthew W.; Van Regenmortel, Marc H. V.
CORPORATE SOURCE: Lab. Immunochim., Inst. de Biol. Mol. Cell., Strasbourg, F-67084, Fr.
SOURCE: European Journal of Immunology (1987), 17(9), 1359-65
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the present study, a quant. immunoassay for cyclophilin was developed which made it possible to compare its relative affinity for cyclosporine and any of its analogs. The binding of cyclophilin to cyclosporine coated on a solid phase was revealed by anticyclophilin rabbit antiserum followed by antiglobulin-enzyme conjugate. This reaction was inhibited by addition of free cyclosporine or certain cyclosporine analogs. By studying the binding of cyclophilin to more than 50 cyclosporine derivs. modified singly on each of the 11 amino acid residues, it was shown that cyclophilin binds to the residues of cyclosporine known to be critical for its immunosuppressive activity. Thus, cyclophilin as a highly

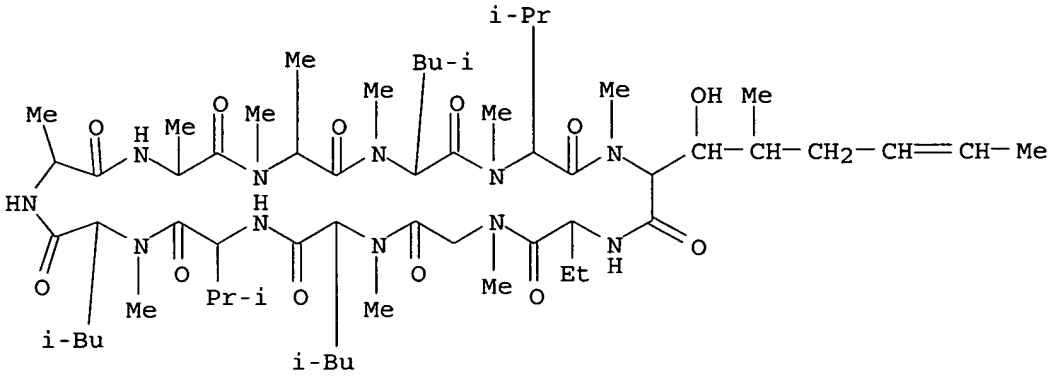
discriminating stereospecific binding protein for cyclosporine.

IT **105300-13-8**

RL: BIOL (Biological study)
(cyclophilin binding to, specificity of, immunosuppression in relation to)

RN 105300-13-8 HCAPLUS

CN Cyclosporin A, 3-(N-methyl-D-alanine)- (9CI) (CA INDEX NAME)



L27 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1988:36050 HCAPLUS

DOCUMENT NUMBER: 108:36050

TITLE: Fine specificity and cross-reactivity of monoclonal antibodies to cyclosporine

AUTHOR(S): Quesniaux, Valerie F. J.; Tees, Reet; Schreier, Max H.; Wenger, Roland M.; Van Regenmortel, Marc H. V.

CORPORATE SOURCE: Sandoz Ltd., Basel, CH-4002, Switz.

SOURCE: Molecular Immunology (1987), 24(11), 1159-68
CODEN: MOIMD5; ISSN: 0161-5890

DOCUMENT TYPE: Journal

LANGUAGE: English

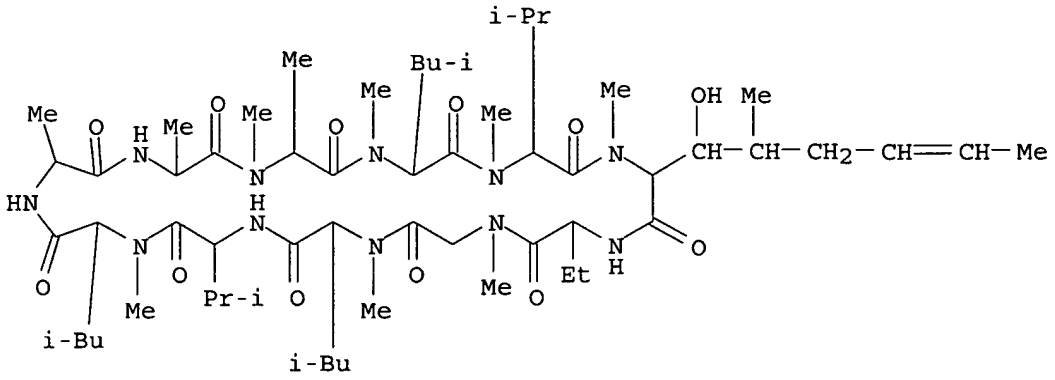
AB More than 180 monoclonal antibodies (McAbs) to the cyclic undecapeptide cyclosporine (Cs) have been prepared Several immunization protocols and antibody screening processes were compared. Two main groups of McAbs recognizing different sides of the Cs mol. could be differentiated. The antibodies belonged to the IgG and IgA classes and showed high affinity for Cs. Based on their ability to discriminate Cs-derivs. modified singly at each of the 11 residues of the Cs mol., the antigenic recognition pattern of different McAbs was studied at the level of individual residues. Closely related recognition patterns were found in each of the 2 main McAb groups. The apparent size of the Cs antigenic sites recognized by different McAbs varied from 4-10 residues and did not correlate with antibody affinity.

IT **112067-18-2**

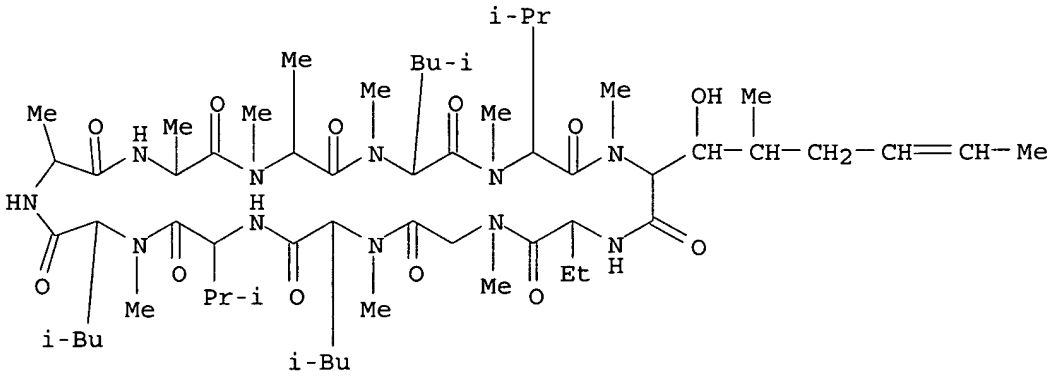
RL: BIOL (Biological study)
(cyclosporine-specific monoclonal antibodies cross-reactivity with)

RN 112067-18-2 HCAPLUS

CN Cyclosporin A, 3-(N-methyl-L-alanine)- (9CI) (CA INDEX NAME)



L27 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:618544 HCAPLUS
DOCUMENT NUMBER: 105:218544
TITLE: Fine specificity of monoclonal antibodies by cyclosporine
AUTHOR(S): Quesniaux, V.; Tees, R.; Schreier, M. H.; Wenger, R. M.; Van Regenmortel, M. H. V.
CORPORATE SOURCE: Preclin. Res., Sandoz Ltd., Basel, CH-4002, Switz.
SOURCE: Transplantation Proceedings (1986), 18(4), 777-9
CODEN: TRPPA8; ISSN: 0041-1345
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The reactivity of monoclonal antibodies to cyclosporine with 50 cyclosporine derivs. was tested. The monoclonal antibodies were found to discriminate between chemical defined cyclosporine derivs. showing only minor structural changes.
IT **105300-13-8**
RL: BIOL (Biological study)
(monoclonal antibodies to cyclosporine reactivity with)
RN 105300-13-8 HCAPLUS
CN Cyclosporin A, 3-(N-methyl-D-alanine)- (9CI) (CA INDEX NAME)



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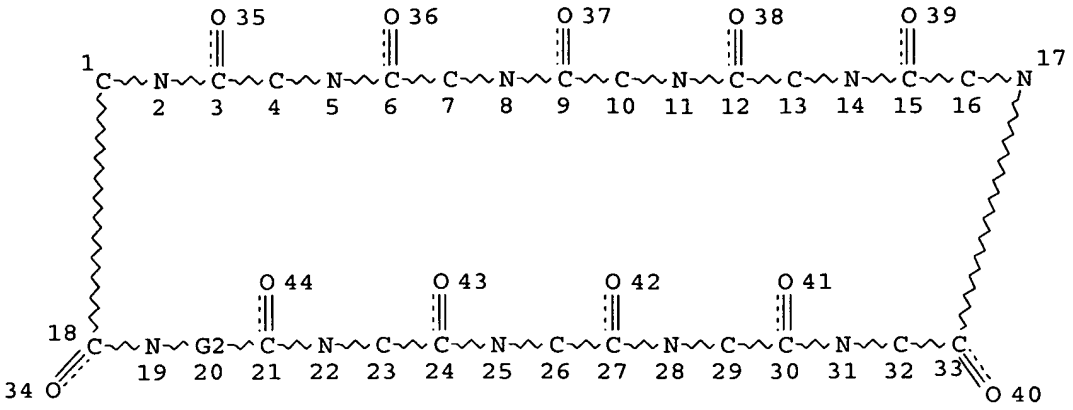

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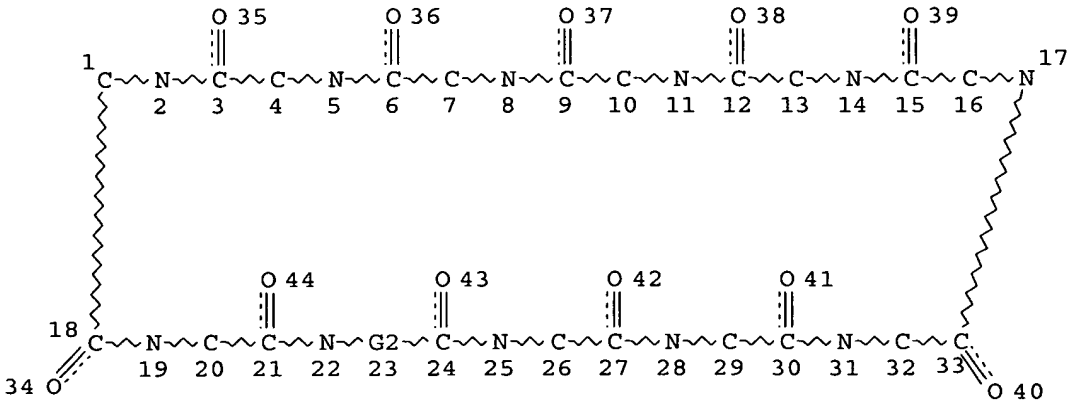
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 49

STEREO ATTRIBUTES: NONE
L2 STR

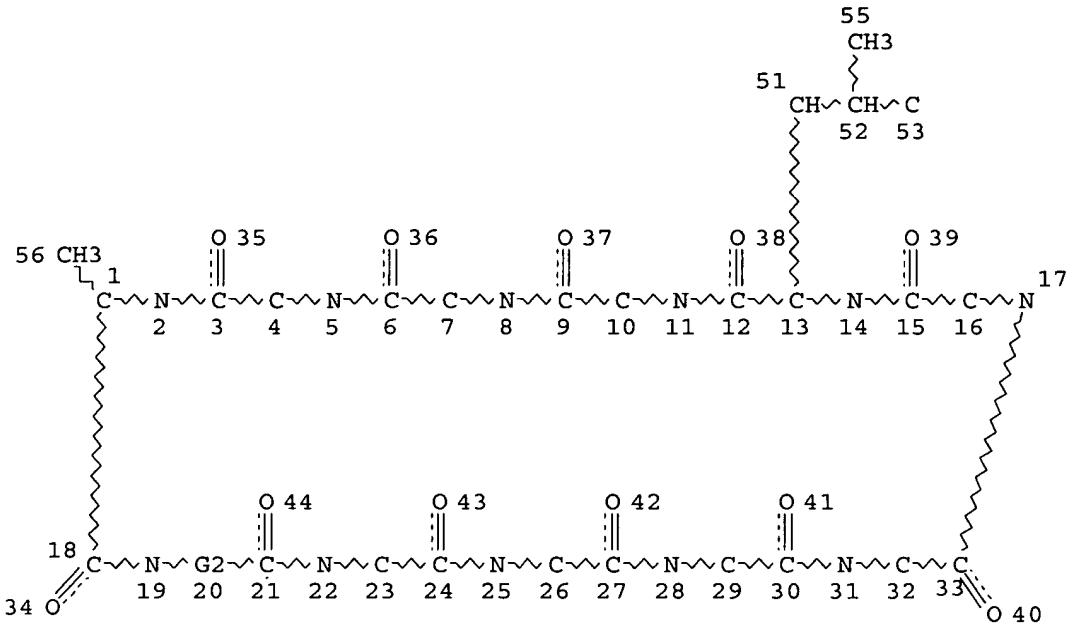


CH CH3 CH2 CH2 CH2
@45 46 @47 48 @49

VAR G2=45/47-22 49-24
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 49

STEREO ATTRIBUTES: NONE
L3 1666 SEA FILE=REGISTRY SSS FUL L1 OR L2
L8 STR

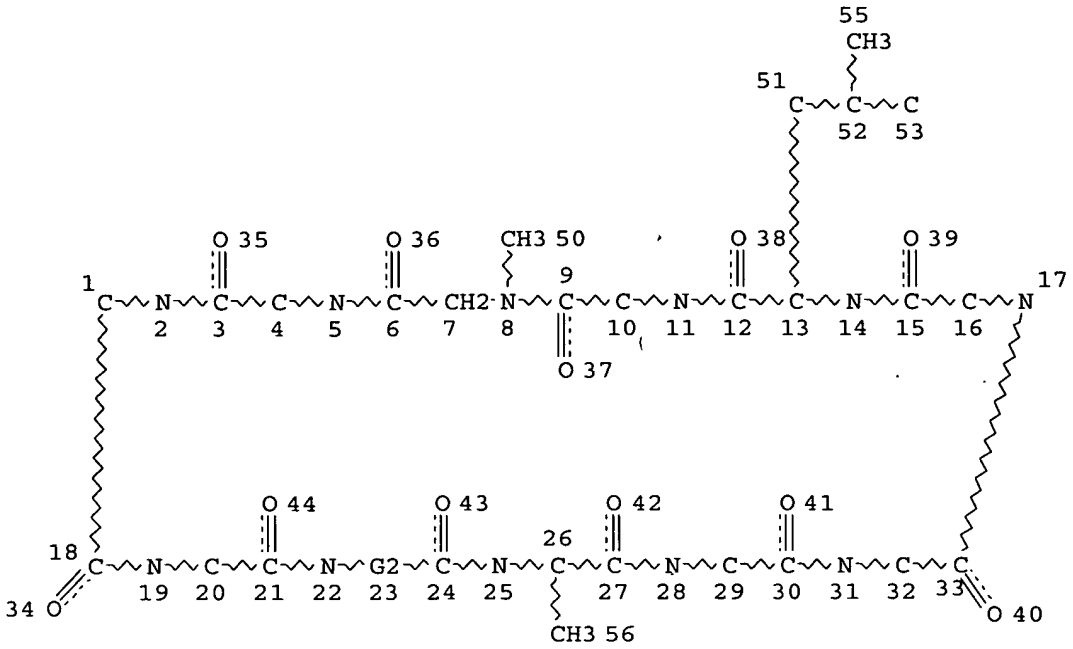


CH CH3 CH2 CH2 CH2
@45 46 @47 48 @49

VAR G2=45/47-19 49-21
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 54

STEREO ATTRIBUTES: NONE
L22 STR



CH CH3 CH2 CH2 CH2
@45 46 @47 48 @49

VAR G2=45/47-22 49-24
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 55

STEREO ATTRIBUTES: NONE
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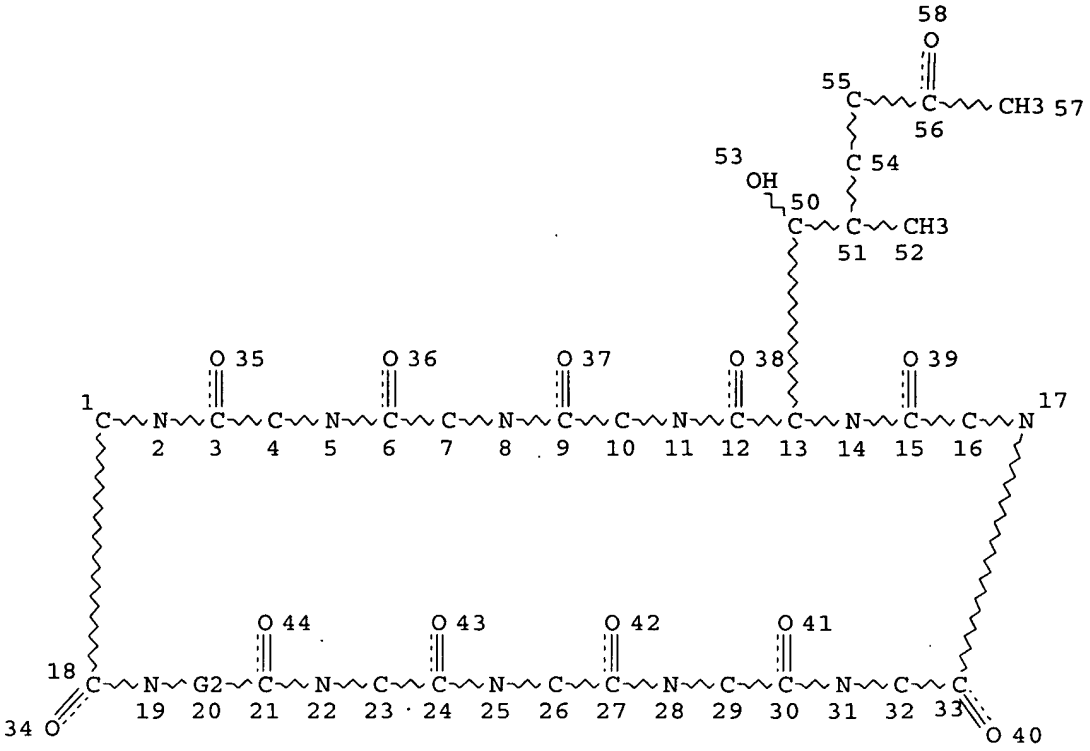
L27 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L23
L28 STR



Page 1-A

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 CH CH3       CH2 CH2 CH2
@45 46       @47 48 @49
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Page 2-A
VAR G2=45/47-19 49-21
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 58

STEREO ATTRIBUTES: NONE
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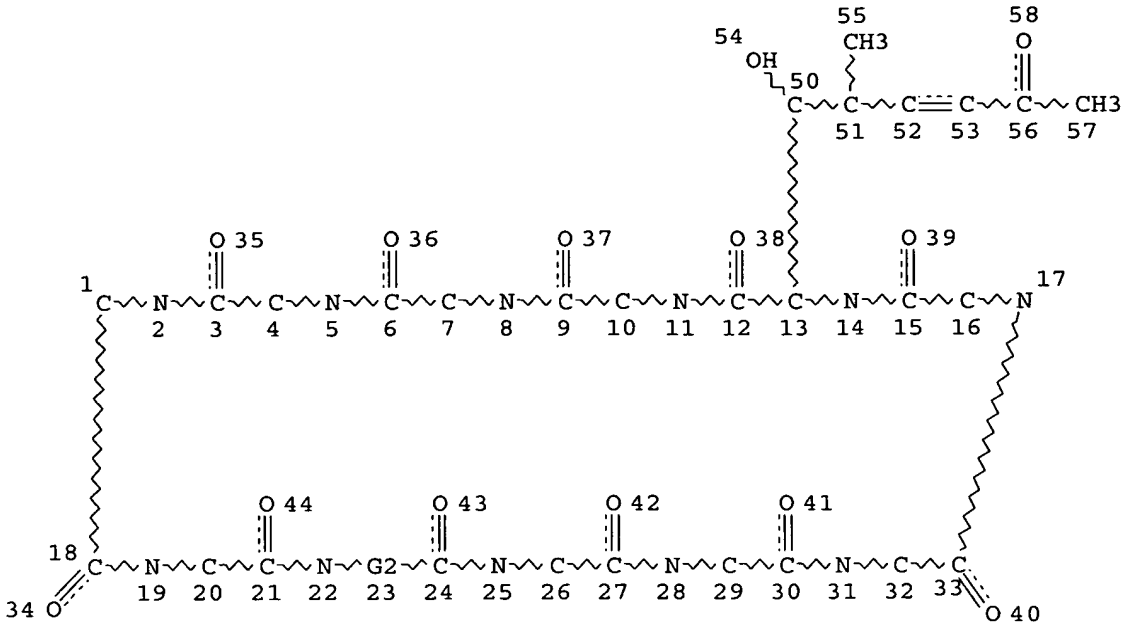

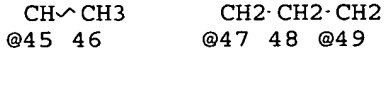

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STEREO ATTRIBUTES: NONE
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L33  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2004:799453  HCAPLUS
DOCUMENT NUMBER:          141:296297
TITLE:                    Preparation of novel cyclosporins
INVENTOR(S):              Molino, Bruce F.; Haydar, Simon N.; Yang, Zhicai;
                          Michels, Peter C.; Hemenway, Michael S.; Rich, Joseph
                          O.; Khmelnitsky, Yuri
PATENT ASSIGNEE(S):       Albany Molecular Research, Inc., USA
SOURCE:                   PCT Int. Appl., 249 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
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LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004082629	A2	20040930	WO 2004-US8118	20040316
WO 2004082629	A3	20051201		
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RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2518265	AA	20040930	CA 2004-2518265	20040316
US 2004235716	A1	20041125	US 2004-802013	20040316
EP 1603512	A2	20051214	EP 2004-757551	20040316
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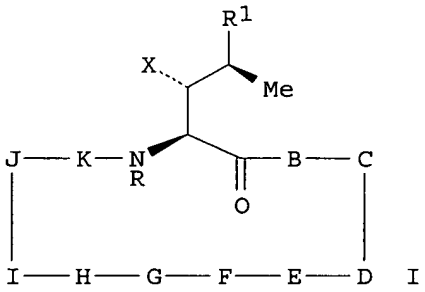
PRIORITY APPLN. INFO.: US 2003-455727P P 20030317
WO 2004-US8118 W 20040316

OTHER SOURCE(S): MARPAT 141:296297
GI



I

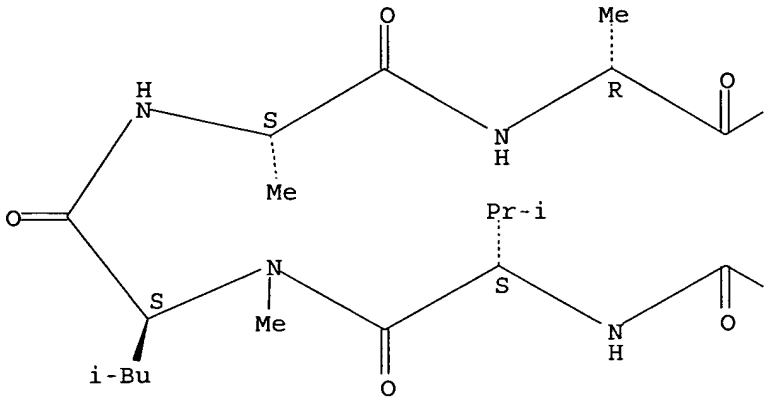
AB The invention relates cyclic peptides I [X is H, OH or a hydroxy group derivatized with an alkanoyl, aryloyl, alkyl-, aryl- or arylalkylaminocarbonyl or -oxycarbonyl group; R is H or Me; R1 is H, CHO, CH:CHCOMe, etc.; B, C, D, E, F, G, H, I, J, and K are certain amino acid residues] or their pharmaceutically-acceptable salts. Thus, cyclosporin A was converted to cyclosporin A Me vinyl ketone [R1 = (E)-2-butenyl to R1 = (E)-3-oxo-1-butenyl] by a biocatalytic method (HOBT-mediated laccase oxidation) or chemical methods using N-hydroxyphthalimide and benzoyl peroxide or tert-Bu hydroperoxide and sodium periodate.

IT **761448-79-7P**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of novel cyclosporins)

RN 761448-79-7 HCAPLUS
CN Cyclosporin A, 6-[(2S,3R,4R,5E)-3-hydroxy-4-methyl-2-(methylamino)-7-oxo-5-octenoic acid]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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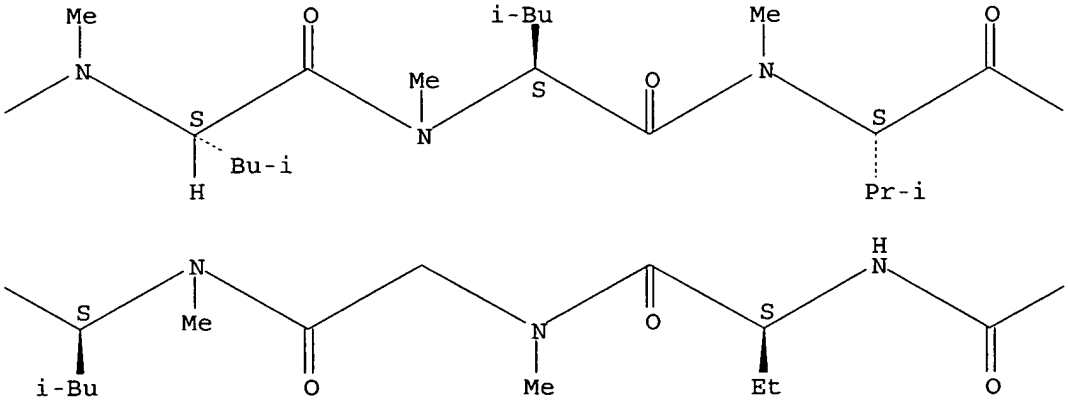

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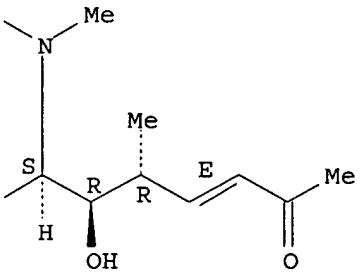

IT **761448-86-6P 761448-87-7P**
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel cyclosporins)
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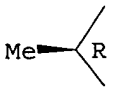
CN Cyclosporin A, 6-[(2S,3R,4R,5E)-3-hydroxy-4-methyl-2-(methylamino)-7-oxo-5-octenoic acid]-9-(4-hydroxy-N-methyl-L-leucine)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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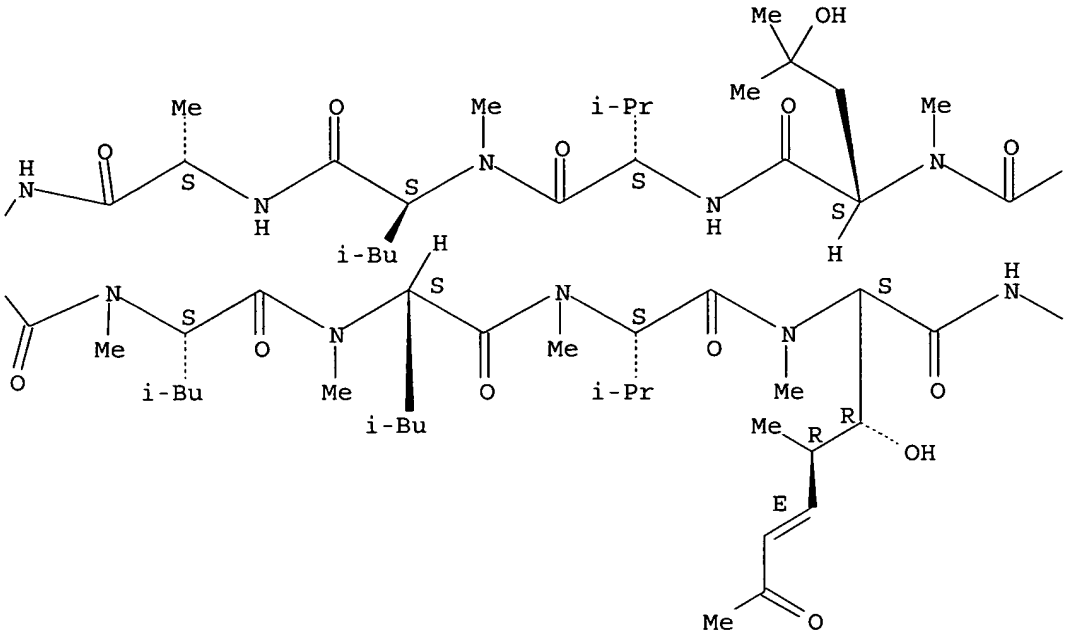

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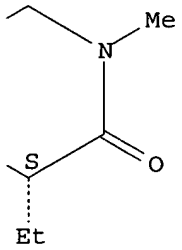
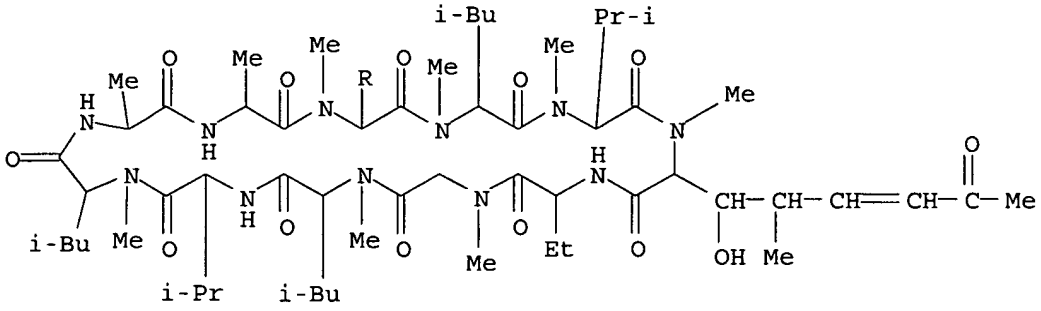
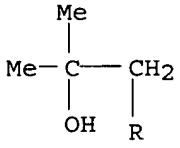


RN 761448-87-7 HCAPLUS
CN Cyclosporin A, 3-(4-hydroxy-N-methyl-L-leucine)-6-[(2S,3R,4R,5E)-3-hydroxy-4-methyl-2-(methylamino)-7-oxo-5-octenoic acid]- (9CI) (CA INDEX NAME)





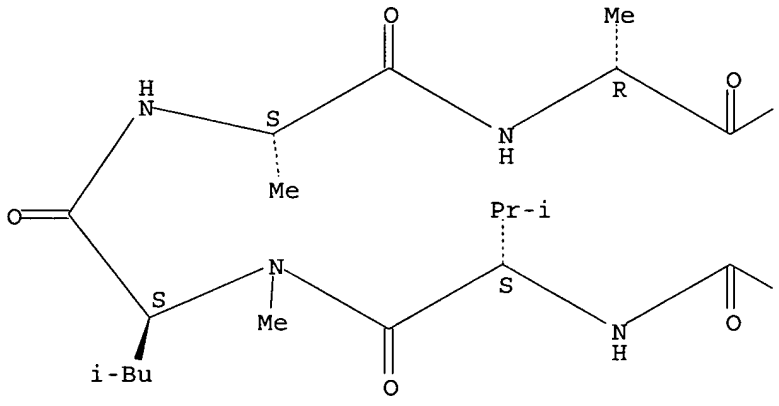
IT **761448-83-3P 761448-84-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of novel cyclosporins)

RN 761448-83-3 HCAPLUS

CN Cyclo[L-alanyl-D-alanyl-N-methyl-L-leucyl-N-methyl-L-leucyl-N-methyl-L-valyl-(2S,3R,4R,5E)-3-hydroxy-4-methyl-2-(methylamino)-7-oxo-5-octenoyl-L-threonyl-N-methylglycyl-N-methyl-L-leucyl-L-valyl-N-methyl-L-leucyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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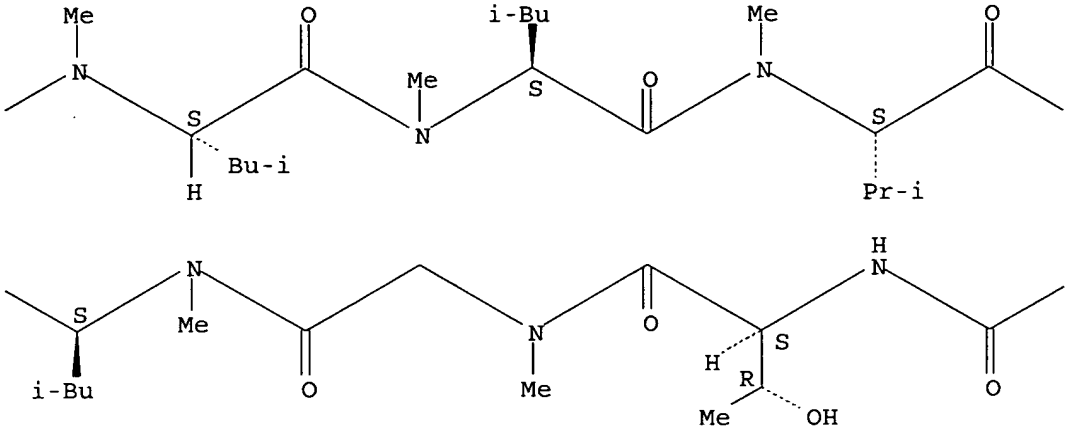

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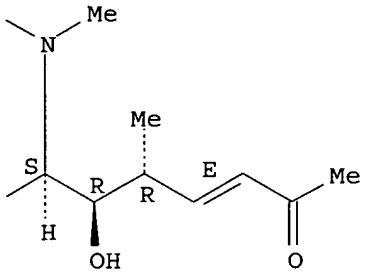
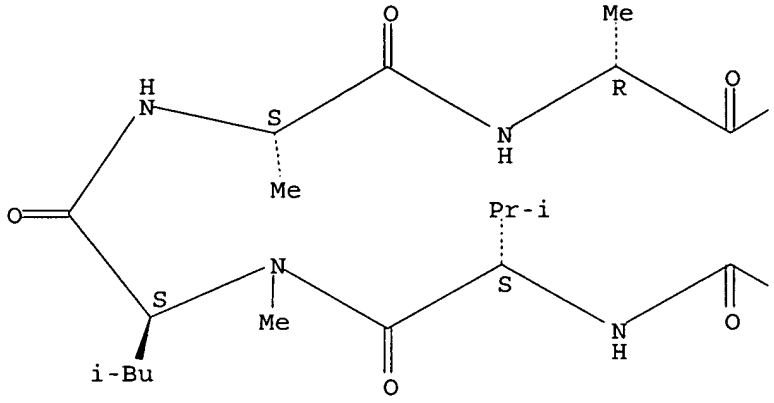


RN 761448-84-4 HCAPLUS
CN Cyclo[L-alanyl-D-alanyl-N-methyl-L-leucyl-N-methyl-L-leucyl-N-methyl-L-valyl-(2S,3R,4R,5E)-3-hydroxy-4-methyl-2-(methylamino)-7-oxo-5-octenoyl-L-valyl-N-methylglycyl-N-methyl-L-leucyl-L-valyl-N-methyl-L-leucyl] (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



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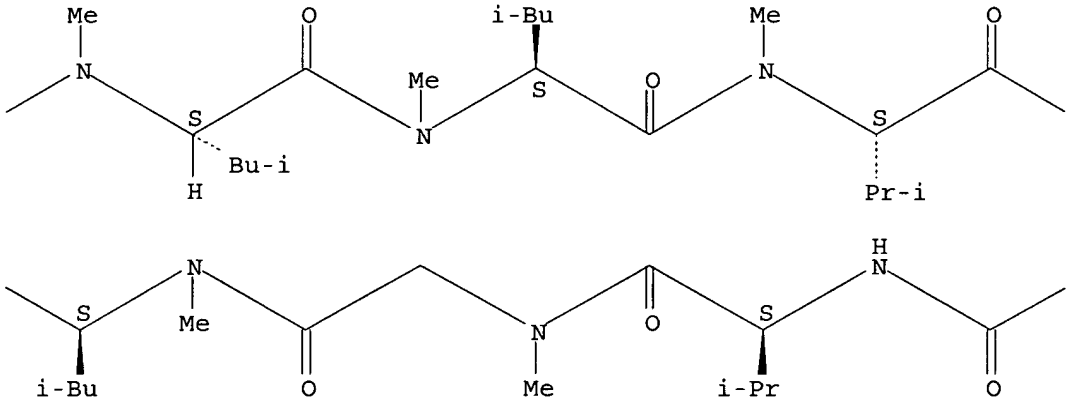

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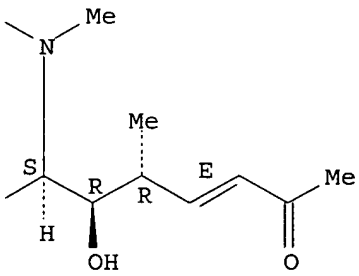

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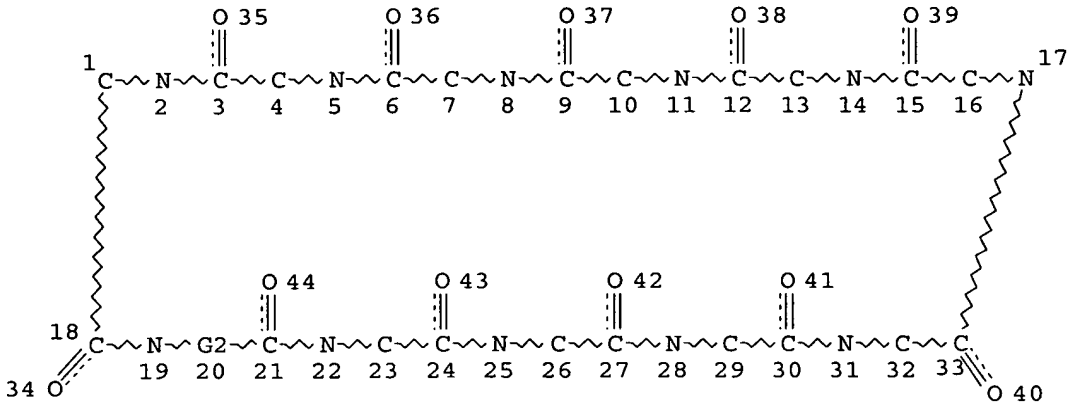


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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  49

STEREO ATTRIBUTES: NONE
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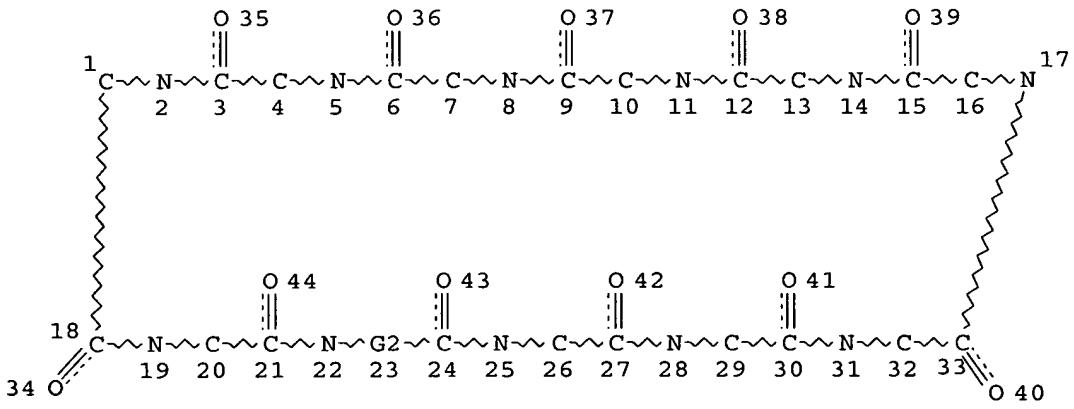


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VAR G2=45/47-22 49-24
NODE ATTRIBUTES:
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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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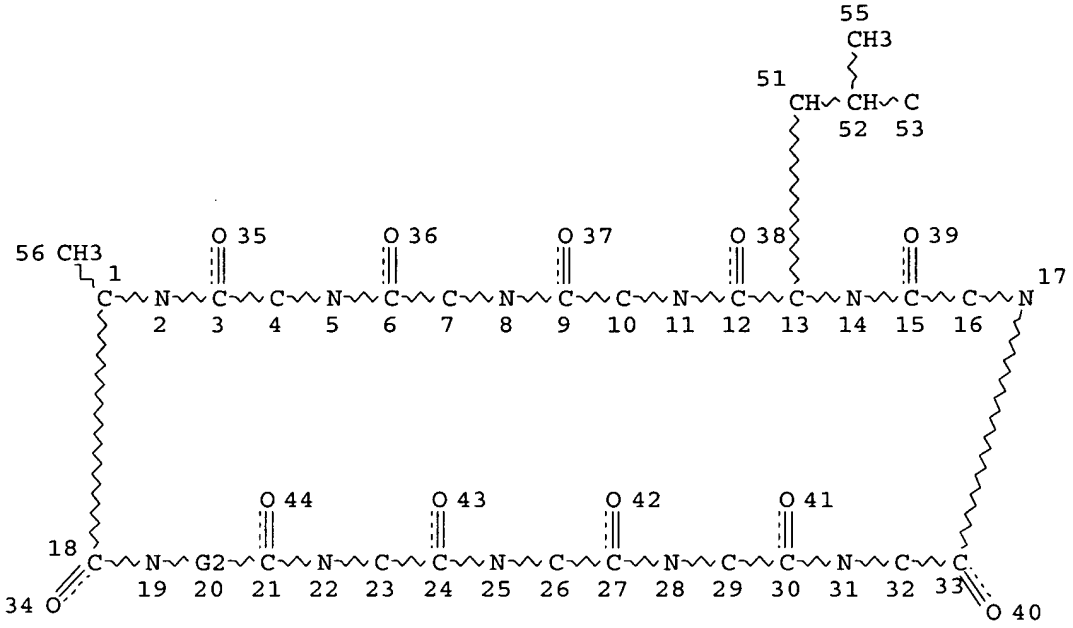

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VAR G2=45/47-19 49-21
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
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STEREO ATTRIBUTES: NONE
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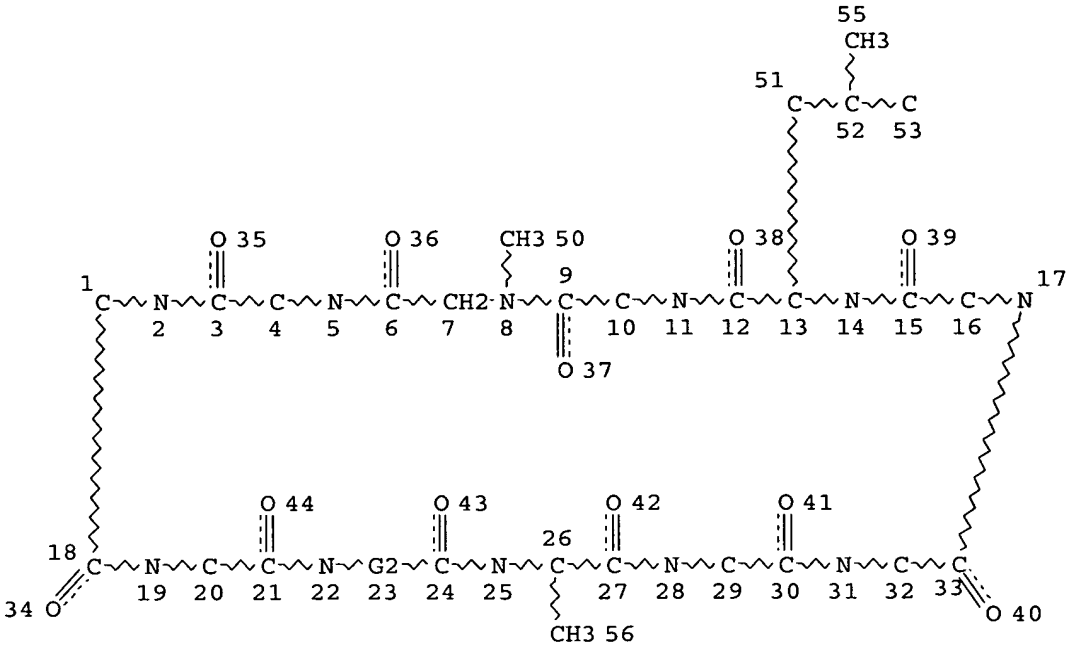

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VAR G2=45/47-22 49-24
NODE ATTRIBUTES:
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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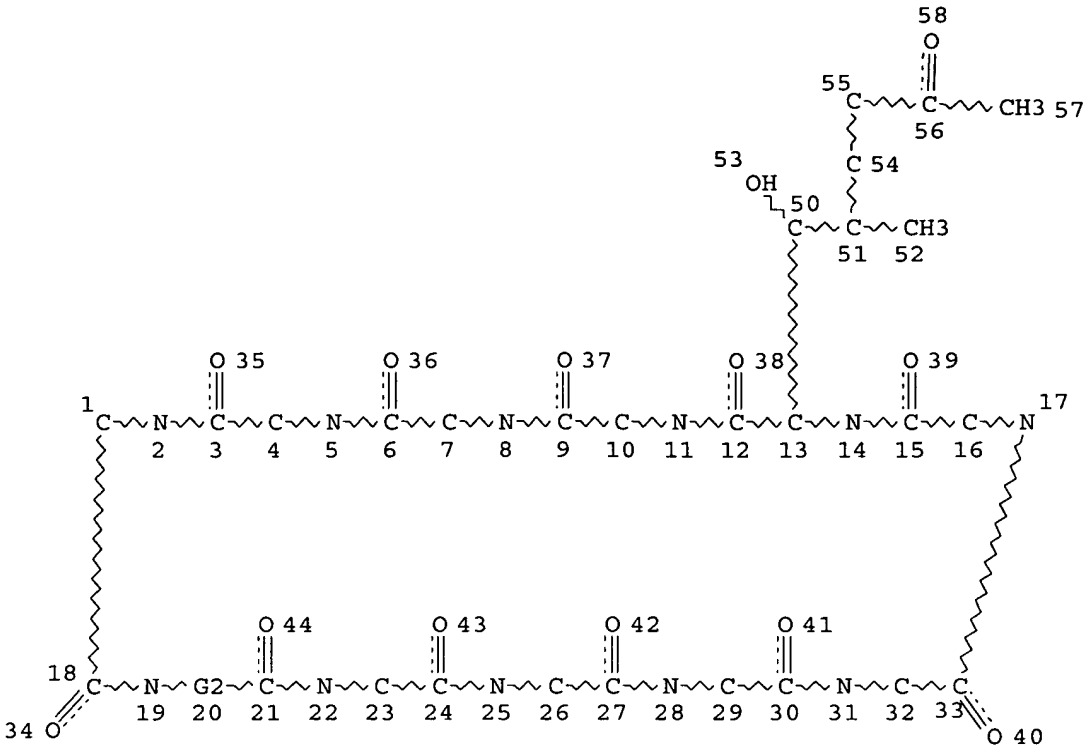

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Page 2-A
VAR G2=45/47-19 49-21
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 58

STEREO ATTRIBUTES: NONE
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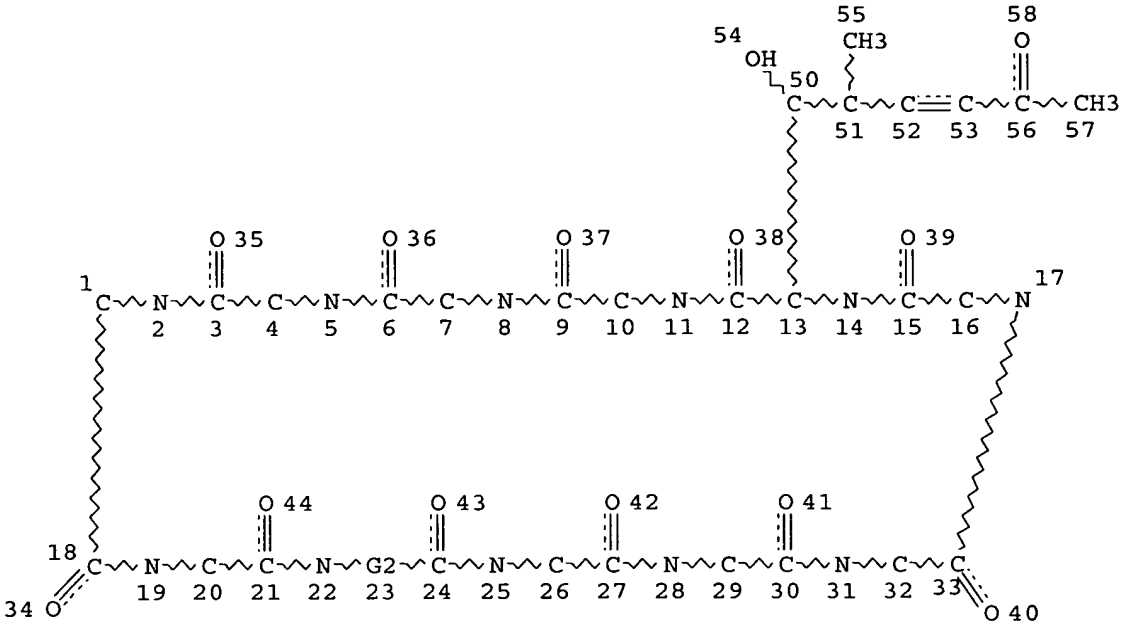

CH~CH3 CH2-CH2-CH2
@45 46 @47 48 @49

VAR G2=45/47-22 49-24
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 58

STEREO ATTRIBUTES: NONE
L30 5 SEA FILE=REGISTRY SUB=L3 SSS FUL L28 OR L29
L31 5 SEA FILE=REGISTRY ABB=ON PLU=ON L30 NOT L23
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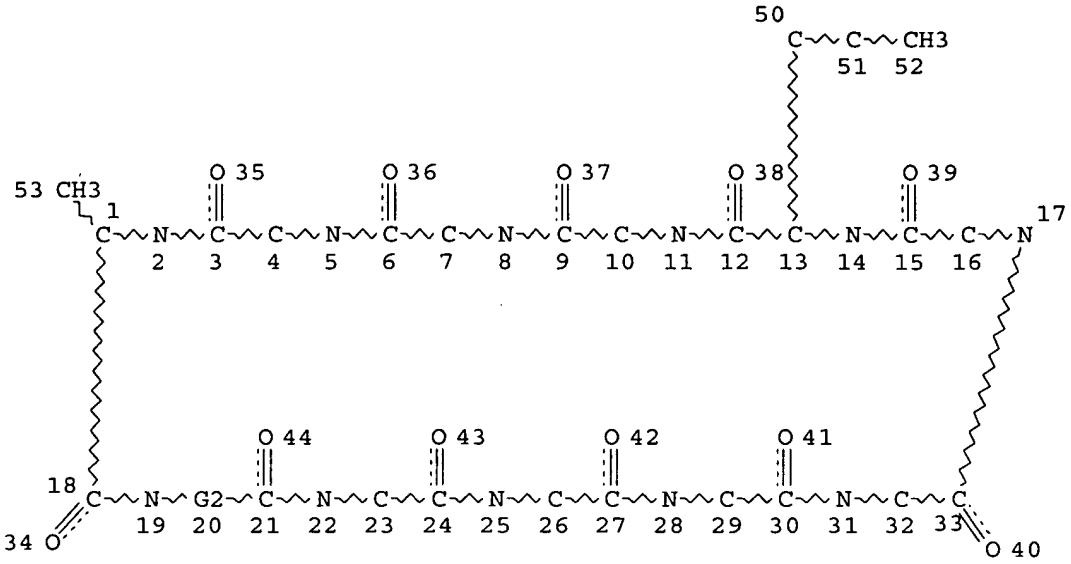
L39 STR



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@45 46 @47 48 @49

VAR G2=45/47-19 49-21
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

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RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 53

STEREO ATTRIBUTES: NONE
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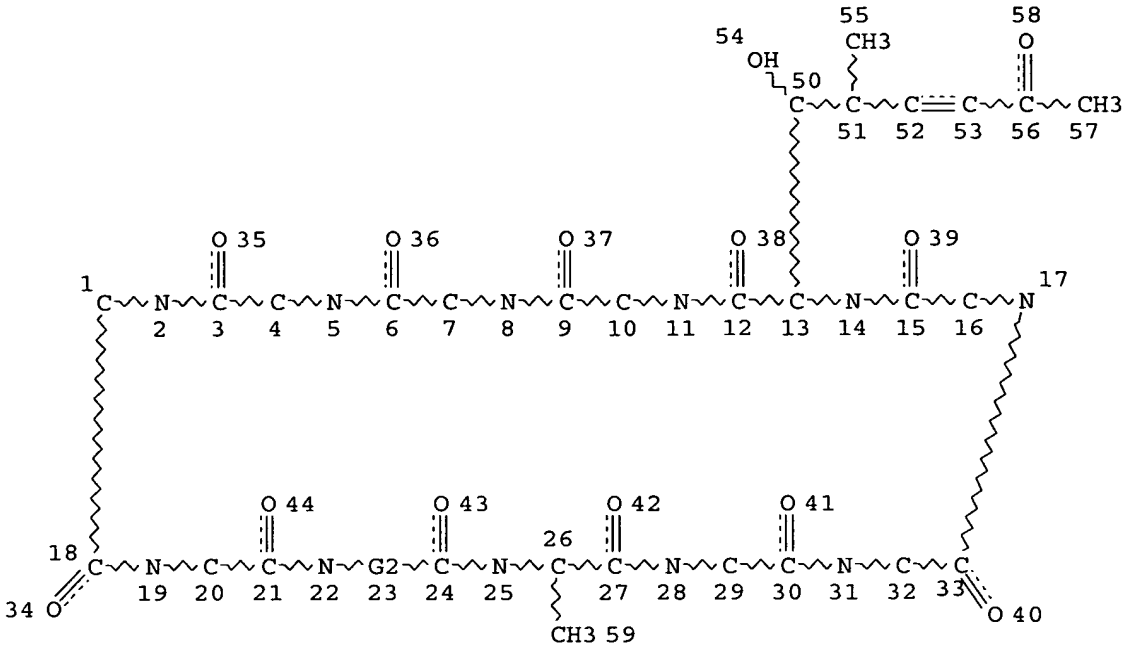

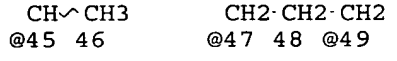

VAR G2=45/47-22 49-24
NODE ATTRIBUTES:
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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 59

STEREO ATTRIBUTES: NONE
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L44 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:888508 HCAPLUS
DOCUMENT NUMBER: 137:389029
TITLE: Use of 3-position cyclosporin derivatives for hair growth
INVENTOR(S): Kim, Sang-Nyun; Ahn, Ho-Jeong; Lee, Chang-Woo; Lee, Min-Ho; Kim, Jung-Hun; Kim, Jong-Il; Kim, Seung-Jin; Cho, Ho-Song; Lee, Heon-Sik; Kim, Hyung-Jin

PATENT ASSIGNEE(S): LG Household & Health Care Ltd., S. Korea
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002092032	A1	20021121	WO 2002-KR879	20020511
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
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CA 2446971	AA	20021121	CA 2002-2446971	20020511
EP 1387660	A1	20040211	EP 2002-728237	20020511
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BR 2002009619	A	20040330	BR 2002-9619	20020511
CN 1507339	A	20040623	CN 2002-809675	20020511
TR 200301931	T2	20040921	TR 2003-200301931	20020511
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US 6762164	B2	20040713		
ZA 2003008532	A	20040701	ZA 2003-8532	20031031
PRIORITY APPLN. INFO.:			KR 2001-25682 A	20010511
			US 2002-141723 A3	20020509
			WO 2002-KR879 W	20020511

OTHER SOURCE(S): MARPAT 137:389029

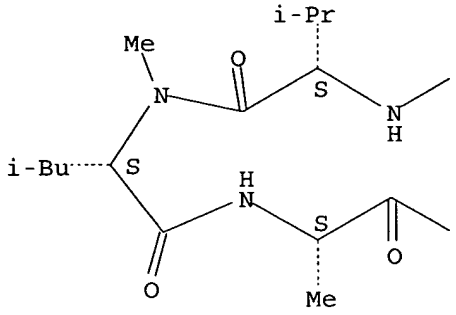
AB The present invention discloses a hair growth promoting agent comprising a cyclosporin derivative as an active ingredient, and more particularly, a hair growth promoting agent comprising a cyclosporin A derivative substituted in the 3-position as an active ingredient. [N-methyl-D-Abu3]cyclosporin A was prepared by alkylation of cyclosporin A with EtI and the compound formulated in a hair tonic.

IT **475637-01-5P**
RL: COS (Cosmetic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(use of 3-position cyclosporin derivs. for hair growth)

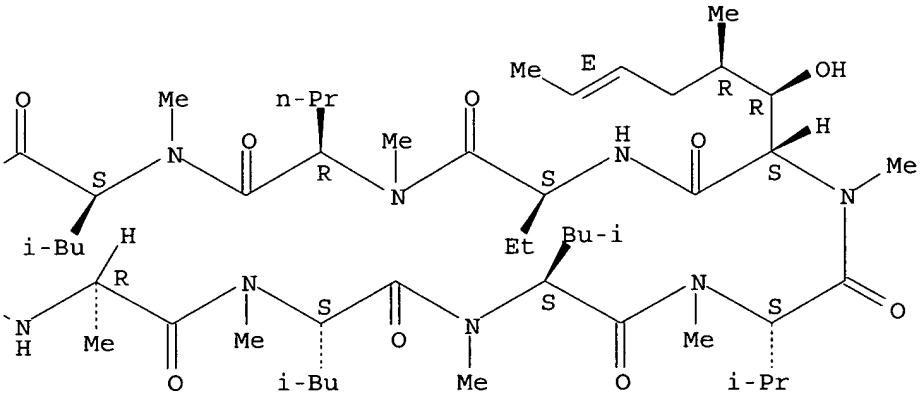
RN 475637-01-5 HCAPLUS
CN Cyclosporin A, 8-(N-methyl-D-norvaline)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

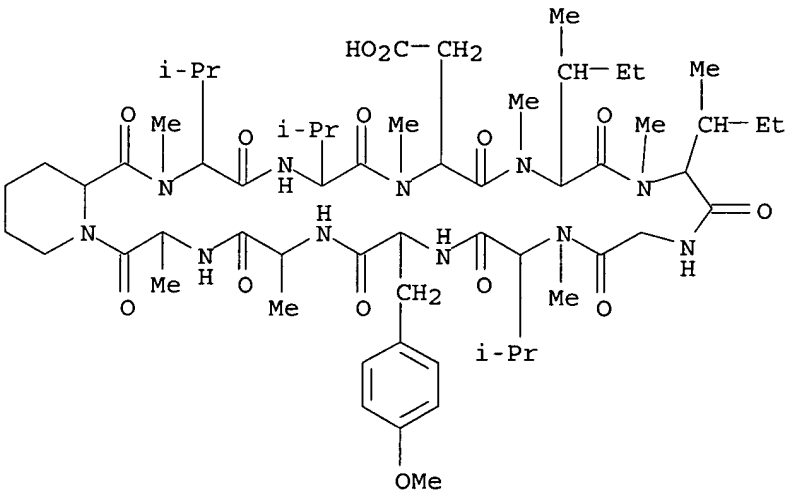
L44 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:13713 HCAPLUS
DOCUMENT NUMBER: 122:10532
TITLE: Derivatives of a Novel Cyclopeptolide. 2. Synthesis, Activity against Multidrug Resistance in CHO and KB Cells in vitro, and Structure-Activity Relationships
AUTHOR(S): Emmer, Gerhard; Grassberger, Maximilian A.; Schulz, Gerhard; Boesch, Danielle; Gaveriaux, Claire; Loor, Francis
CORPORATE SOURCE: Department of Dermatology, SANDOZ Forschungsinstitut, Vienna, A-1235, Austria
SOURCE: Journal of Medicinal Chemistry (1994), 37(13), 1918-28
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of derivs. of the novel antifungal cyclopeptolide cyclo[Pec1-MeVal2-Val3-MeAsp4-MeIle5-MeIle6-Gly7-MeVal8-Tyr(Me)9-(R)-

Lac10], (1; Pec = L-pipecolic acid, Lac = lactic acid) was prepared, and their ability to chemosensitize multi drug resistant CHO and KB cells in vitro was evaluated. In contrast to the parent compound, several of the derivs. were highly active. In particular, conversion of the R-lactic acid residue of 1 into its S-isomer via lactone ring cleavage and recyclization with inversion resulted in a marked enhancement of activity. Some of these derivs., e.g. cyclo[Pec-MeVal-Val-MeAsp(OCMe3)-MeIle-MeIle-Gly-MeVal-Tyr(Me)-(S)-Lac] (SDZ 280.446) belong to the most potent resistance modulating compds. known so far.

IT **159105-13-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(drug resistance modulating activity of)

RN 159105-13-2 HCAPLUS

CN Cyclo[D-alanyl-L-alanyl-(2S)-2-piperidinecarbonyl-N-methyl-L-valyl-L-valyl-N-methyl-L-α-aspartyl-N-methyl-L-isoleucyl-N-methyl-L-isoleucylglycyl-N-methyl-L-valyl-O-methyl-L-tyrosyl] (9CI) (CA INDEX NAME)



L44 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:13712 HCAPLUS

DOCUMENT NUMBER: 122:10531

TITLE: Derivatives of a Novel Cyclopeptolide. 1. Synthesis, Antifungal Activity, and Structure-Activity Relationships

AUTHOR(S): Emmer, Gerhard; Grassberger, Maximilian A.; Meingassner, Josef G.; Schulz, Gerhard; Schaude, Michael

CORPORATE SOURCE: Department of Dermatology, SANDOZ Forschungsinstitut, Vienna, A-1235, Austria

SOURCE: Journal of Medicinal Chemistry (1994), 37(13), 1908-17
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The synthesis of a series of derivs. of the novel antifungal cyclopeptolide cyclo[Pec1-MeVal2-Val3-MeAsp4-MeIle5-MeIle6-Gly7-MeVal8-Tyr(Me)9-(R)-Lac10], (1; Pec = L-pipecolic acid, Lac = lactic acid), is described. Besides functional group variation of MeAsp4 (esters, amides, and alc. derivs.) and Tyr(Me)9 derivs., opening of the lactone by LiOH in

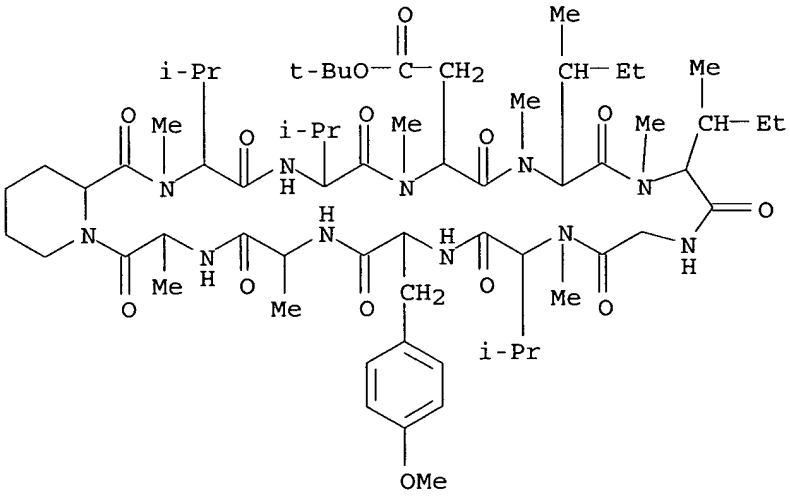
THF/H2O allowed manipulation of the hydroxy group of (R)-Lac10 in the resulting acyclic peptide 15. Recyclization of 15 under Mitsunobu conditions followed by deprotection led to the (S)-Lac10 analog. Cyclic decapeptides, as well as cyclic undecapeptides, were obtained via corresponding modified linear peptides by cyclization. Methylation of all secondary amide groups by MeI and KH/18-crown-6 gave the permethylated compound Two derivs., cyclo[Pec1-MeVal2-Val3-MeAsp4-MeIle5-MeIle6-Gly7-MeVal8-Tyr(Me)9-X10] [X10 = (S)-Lac, D-Ala], showed superior activities against yeasts in vitro at pH 6.5 as compared to 1, but not at a lower pH (4.5).

IT **129816-82-6P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation , acidic deesterification, and antifungal activity of)

RN 129816-82-6 HCAPLUS

CN Cyclo[D-alanyl-L-alanyl-(2S)-2-piperidinecarbonyl-N-methyl-L-valyl-L-valyl-N-methyl-L-α-aspartyl-N-methyl-L-isoleucyl-N-methyl-L-isoleucylglycyl-N-methyl-L-valyl-O-methyl-L-tyrosyl], 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

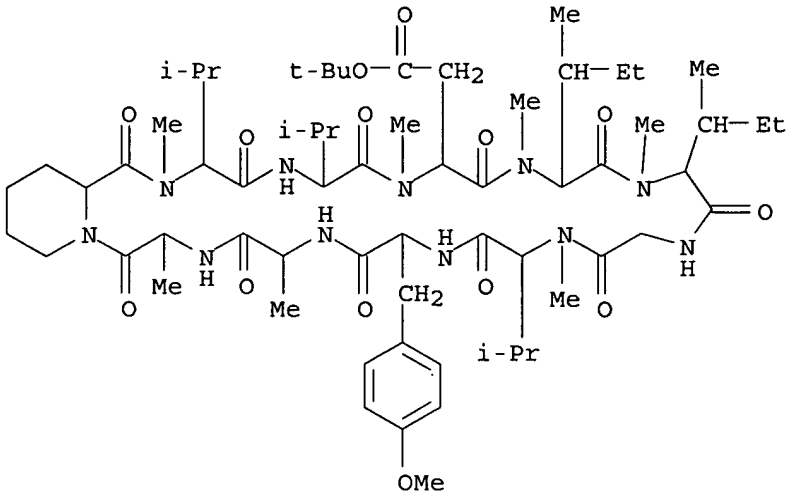


IT **129893-90-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and acidic deesterification of)

RN 129893-90-9 HCAPLUS

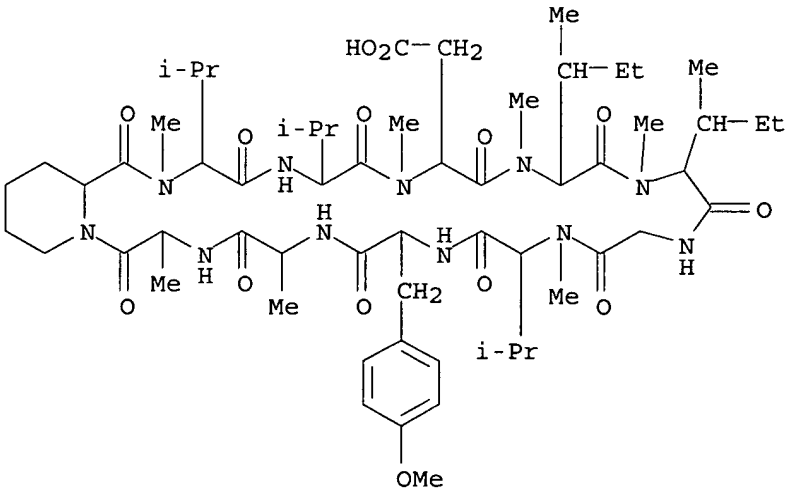
CN Cyclo[D-alanyl-D-alanyl-(2S)-2-piperidinecarbonyl-N-methyl-L-valyl-L-valyl-N-methyl-L-α-aspartyl-N-methyl-L-isoleucyl-N-methyl-L-isoleucylglycyl-N-methyl-L-valyl-O-methyl-L-tyrosyl], 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IT **159105-13-2P 159170-93-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antifungal activity of)

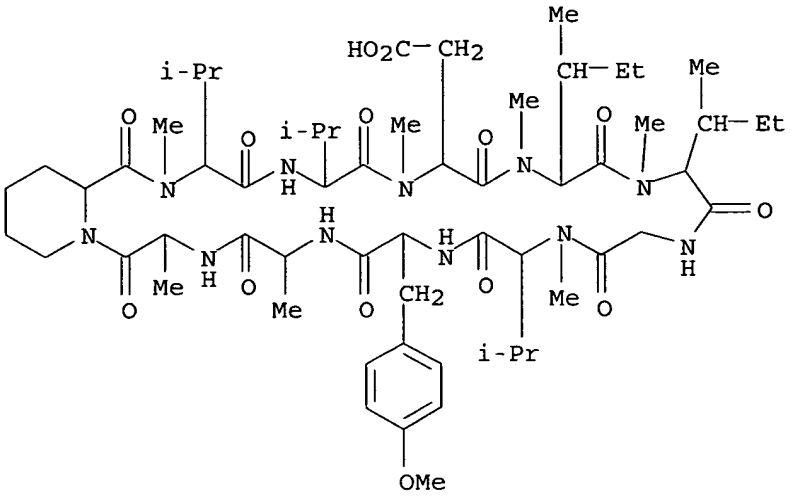
RN 159105-13-2 HCAPLUS

CN Cyclo[D-alanyl-L-alanyl-(2S)-2-piperidinecarbonyl-N-methyl-L-valyl-L-valyl-N-methyl-L-α-aspartyl-N-methyl-L-isoleucyl-N-methyl-L-isoleucylglycyl-N-methyl-L-valyl-O-methyl-L-tyrosyl] (9CI) (CA INDEX NAME)



RN 159170-93-1 HCAPLUS

CN Cyclo[D-alanyl-D-alanyl-(2S)-2-piperidinecarbonyl-N-methyl-L-valyl-L-valyl-N-methyl-L-α-aspartyl-N-methyl-L-isoleucyl-N-methyl-L-isoleucylglycyl-N-methyl-L-valyl-O-methyl-L-tyrosyl] (9CI) (CA INDEX NAME)

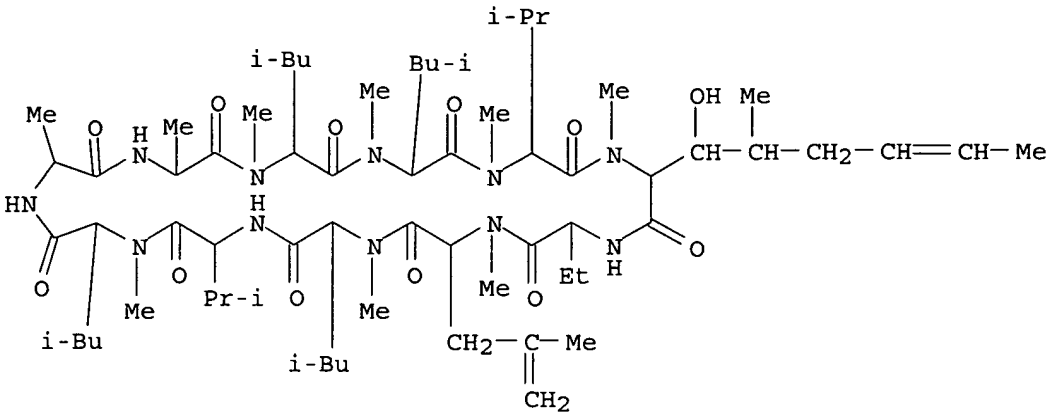


L44 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:671687 HCAPLUS
DOCUMENT NUMBER: 119:271687
TITLE: Modification of cyclosporin A (CS): generation of an enolate at the sarcosine residue and reactions with electrophiles
AUTHOR(S): Seebach, Dieter; Beck, Albert K.; Bossler, Hans G.; Gerber, Christian; Ko, Soo Y.; Murtiashaw, C. William; Naef, Reto; Shoda, Shinichiro; Thaler, Adrian; et al.
CORPORATE SOURCE: Lab. Org. Chem., Eidg. Techn. Hochsch., Zurich, CH-8092, Switz.
SOURCE: Helvetica Chimica Acta (1993), 76(4), 1564-90
CODEN: HCACAV; ISSN: 0018-019X
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 119:271687

AB Strong bases (LDA or BuLi) convert cyclosporin A (CS) to a hexalithio derivative containing a Li alkoxide, four Li azaenolate, and one Li enolate unit.

The Li6 compound is solubilized in THF by addition of excess LDA or LiCl. Reactions with electrophiles (alkyl halides, aldehydes, chloroformates, CO2, disulfides, D2O) at low temps. give products containing new side chains at the sarcosine residue of the cyclic undecapeptide in moderate to high yields and, with Re- or Si-selectivities of up to 7:1, depending upon the lithiation conditions. Pure CS derivs. can be isolated by column chromatog. N-alkylations or cleavage of the peptide backbone by carbonyl addition occur only at higher temps. and/or with prolonged reaction times. Very little or no epimerization of stereogenic centers occurs under the conditions employed. Possible reasons for the feasibility of these surprising conversions of CS are discussed. For comparison, [MeAla3]CS and [D-MeAla3]CS were also prepared by conventional peptide synthesis in solution Their 1H and 13C NMR spectra are compared with those of CS.

IT **108466-56-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, via stereoselective alkylation of cyclosporin A enolate)
RN 108466-56-4 HCAPLUS
CN Cyclosporin A, 8-(4,5-didehydro-N-methyl-D-leucine)- (9CI) (CA INDEX NAME)

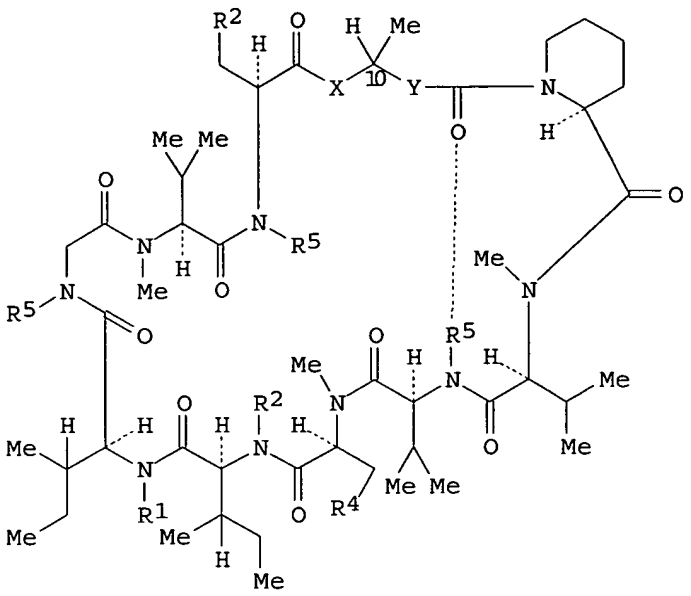


L44 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1990:572754 HCAPLUS
DOCUMENT NUMBER: 113:172754
TITLE: Manufacture and chemical transformations of cyclopeptolides as medical fungicides and neoplasm inhibitor enhancers
INVENTOR(S): Dreyfuss, Michael M.; Emmer, Gerhard; Grassberger, Maximilian; Rueedi, Klaus; Tscherter, Hans
PATENT ASSIGNEE(S): Sandoz-Patent-G.m.b.H., Germany
SOURCE: Ger. Offen., 44 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3832362	A1	19900329	DE 1988-3832362	19880923
HU 51299	A2	19900428	HU 1989-4797	19890908
DK 8904669	A	19900324	DK 1989-4669	19890921
FI 8904480	A	19900324	FI 1989-4480	19890921
EP 360760	A2	19900328	EP 1989-810721	19890921
EP 360760	A3	19901010		
EP 360760	B1	19950215		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
IL 91708	A1	19940530	IL 1989-91708	19890921
ES 2068913	T3	19950501	ES 1989-810721	19890921
CA 1340447	A1	19990316	CA 1989-612370	19890921
AU 8941652	A1	19900405	AU 1989-41652	19890922
AU 628855	B2	19920924		
JP 02134399	A2	19900523	JP 1989-247852	19890922
ZA 8907249	A	19910529	ZA 1989-7249	19890922
US 5643869	A	19970701	US 1995-446983	19950522

PRIORITY APPLN. INFO.:
DE 1988-3832362 A 19880923
US 1989-411336 B1 19890922
US 1992-874277 B1 19920424
US 1994-187929 B1 19940127

OTHER SOURCE(S): CASREACT 113:172754; MARPAT 113:172754
GI



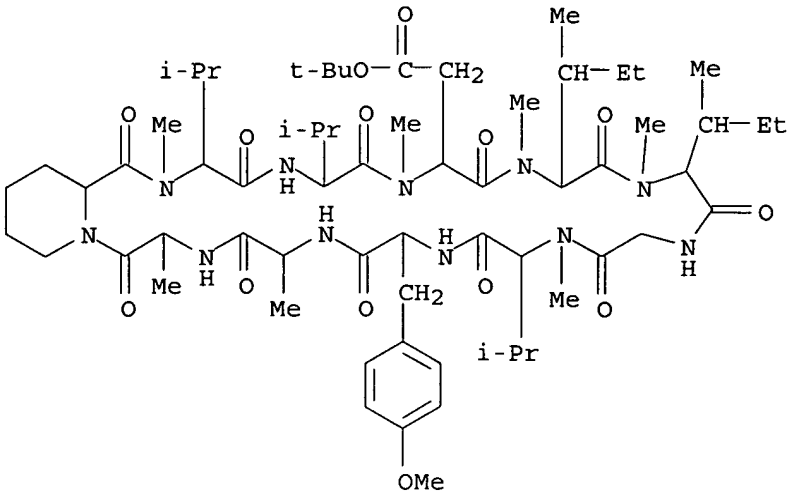
I

AB The title compds. [I; R1, R2, R5 = H, Me; R1, R2 cannot both = H; R3 = R6OC6H4, cyclohexyl, cyclohexenyl, cyclohexadienyl; R4 = COR7, CH2R8, cyano; R6 = H, alkyl, alkenyl, acyl, geranyl, aralkyl, etc.; R7 = H (ar)alkyl, OR9, NR10R11, etc.; R8 = H, halo, alkyl, alkenyl, azido, adamantylcarbonyloxy, naphthylaminocarbonyloxy, etc.; R9 = H, alkyl, alkenyl, aryl, PhCH2, etc.; R10, R11 = H, alkoxy(alkyl), (un)substituted CH2CO2H, furylmethyl, Ph, Ph2CH, etc.; X = O, NH; Y = bond, CONH, CHMe; C-atoms in position 10 have D- or L-config.], specifically I (R3 = 4-MeOC6H4, R4 = CO2H, R5 = H, X = O, Y = bond), were manufactured by harvesting the product of a mycellar suspension of NRRL 15761 and subjecting it to a series of chemical transformations. In vitro, 1.5-25 mg I/mL inhibit fungi, e.g., Candida; in rats, I at 0.1-1% locally gave 100% healing of the intravaginal Candida infection. I enhance the effectiveness of neoplasm inhibitors by restoring the sensitivity of, e.g., carcinoma cells in vivo toward antineoplastic/cyctotoxic drugs.

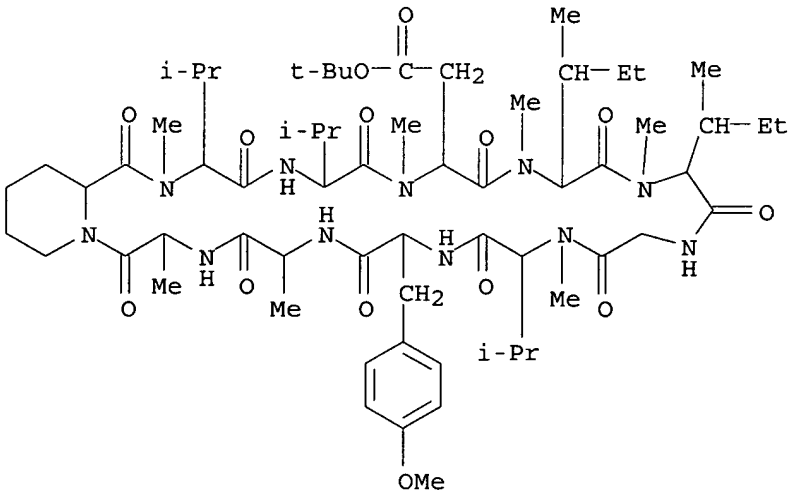
IT **129816-82-6P 129893-90-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as medical fungicide and neoplasm inhibitor enhancer)

RN 129816-82-6 HCAPLUS

CN Cyclo[D-alanyl-L-alanyl-(2S)-2-piperidinecarbonyl-N-methyl-L-valyl-L-valyl-N-methyl-L-α-aspartyl-N-methyl-L-isoleucyl-N-methyl-L-isoleucylglycyl-N-methyl-L-valyl-O-methyl-L-tyrosyl], 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 129893-90-9 HCAPLUS
CN Cyclo[D-alanyl-D-alanyl-(2S)-2-piperidinecarbonyl-N-methyl-L-valyl-L-valyl-N-methyl-L-α-aspartyl-N-methyl-L-isoleucyl-N-methyl-L-isoleucylglycyl-N-methyl-L-valyl-O-methyl-L-tyrosyl], 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L44 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:407610 HCAPLUS
DOCUMENT NUMBER: 107:7610
TITLE: Cyclosporins
INVENTOR(S): Seebach, Dieter
PATENT ASSIGNEE(S): Sandoz A.-G., Switz.; Sandoz-Patent-G.m.b.H.; Sandoz-Erfindungen Verwaltungsgesellschaft m.b.H.
SOURCE: Eur. Pat. Appl., 66 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English

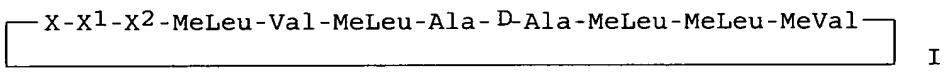
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 194972	A2	19860917	EP 1986-810112	19860306
EP 194972	A3	19890712		
EP 194972	B1	19920729		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 78832	E	19920815	AT 1986-810112	19860306
US 4703033	A	19871027	US 1986-837434	19860307
DK 8601094	A	19860912	DK 1986-1094	19860310
FI 8600993	A	19860912	FI 1986-993	19860310
JP 61212599	A2	19860920	JP 1986-53528	19860310
JP 07059594	B4	19950628		
HU 45272	A2	19880628	HU 1986-1009	19860310
ES 552855	A1	19890116	ES 1986-552855	19860310
ES 552855	A5	19890214		
HU 47137	A2	19890130	HU 1986-1434	19860310
PL 151029	B1	19900731	PL 1986-258350	19860310
PL 151429	B1	19900928	PL 1986-267785	19860310
AU 8654485	A1	19860918	AU 1986-54485	19860311
AU 588860	B2	19890928		
ZA 8601805	A	19871125	ZA 1986-1805	19860311
ES 557619	A1	19880716	ES 1987-557619	19870701
ES 557619	A5	19880816		
US 4771122	A	19880913	US 1987-103990	19871001
AU 8938176	A1	19891102	AU 1989-38176	19890717

PRIORITY APPLN. INFO.:

GB 1985-6230	A	19850311
GB 1985-11029	A	19850501
GB 1986-2370	A	19860131
EP 1986-810112	A	19860306
US 1986-837434	A3	19860307

GI



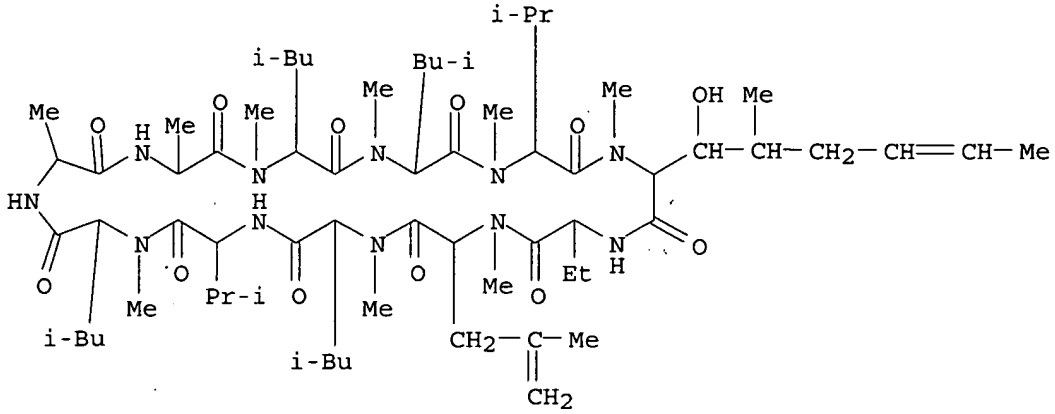
I

AB The title compds. I [X = (dihydro)-N-methyl-4-[(2E,4R)-but-2-en-1-yl]-4-methyl-L-threonyl (MeBmt); X1 = αAbu, Thr, Val, Nva; X2 = NMeCHRCO; R = halo, cyano, CONH2, (un)substituted alkyl, alkylcarbonyl, (un)substituted alkylthio, (un)substituted alkenyl, (hetero)arylthio, etc.], possessing immunosuppressive, antiinflammatory and antiparasitic activity, were prepared by treating cyclosporins with a base and reacting the resulting cyclosporin polyanions having a deprotonated sarcosine residue (I; X2 = sarcosyl) with electrophiles, e.g. aldehydes, isocyanates, disulfides, alkyl halides. Thus, cyclosporin A in THF was added dropwise to 6.7 equiv (Me2CH)2NLi in THF at -78° and after 1 h MeI was added at -78°. The mixture was allowed to warm to room temperature to give I (X = MeBmt; X1 = αAbu; X2 = MeAla). The title compds. at 0.01-10 μg/mL inhibited concanavalin A stimulated DNA synthesis, cell-proliferation and blasto-genesis in mouse spleen lymphocytes and at 1-30 mg/kg/day p.o. were active against arthritis in rats, and at 10-50 mg/kg/day p.o. doubled the survival time of mice infected with malaria.

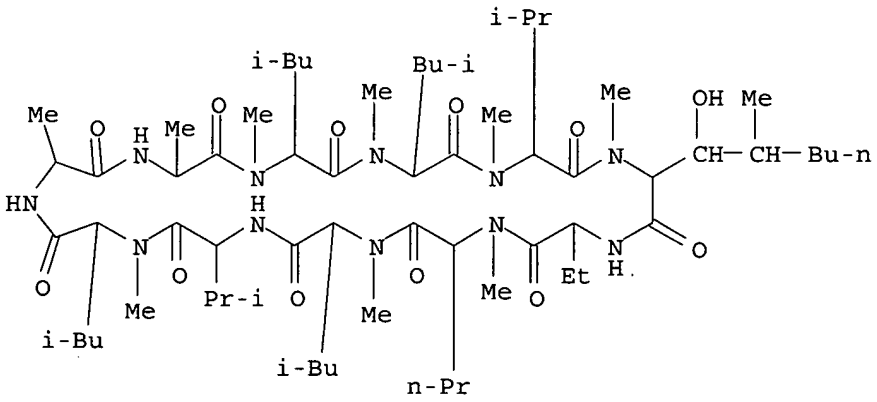
IT **108466-56-4P 108466-74-6P 108466-75-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as immunosuppressive, antiinflammatory, and antiparasitic agent)

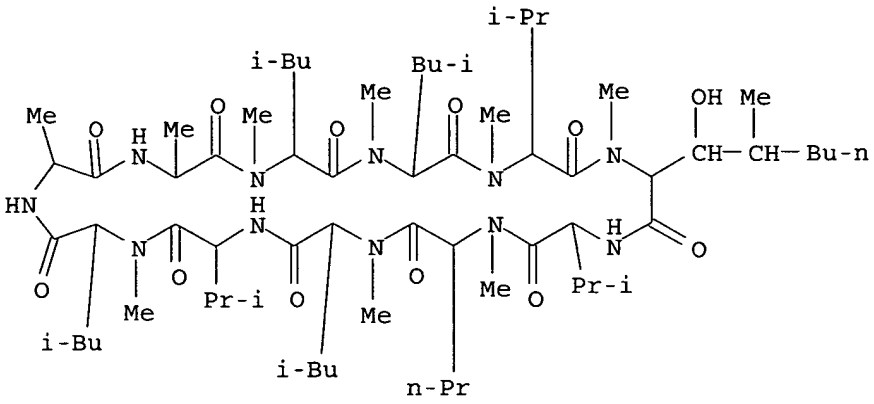
RN 108466-56-4 HCAPLUS
CN Cyclosporin A, 8-(4,5-didehydro-N-methyl-D-leucine)- (9CI) (CA INDEX NAME)



RN 108466-74-6 HCAPLUS
CN Cyclosporin A, 6-[(3R,4R)-3-hydroxy-N,4-dimethyl-L-2-aminooctanoic acid]-8-(N-methyl-D-norvaline)- (9CI) (CA INDEX NAME)



RN 108466-75-7 HCAPLUS
CN Cyclosporin A, 6-[(3R,4R)-3-hydroxy-N,4-dimethyl-L-2-aminooctanoic acid]-7-L-valine-8-(N-methyl-D-norvaline)- (9CI) (CA INDEX NAME)



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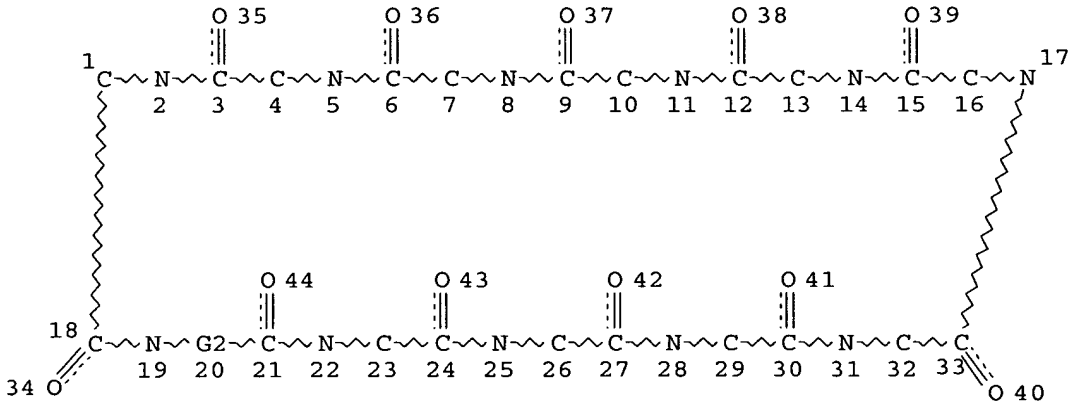
L1 STR



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@45 46 @47 48 @49

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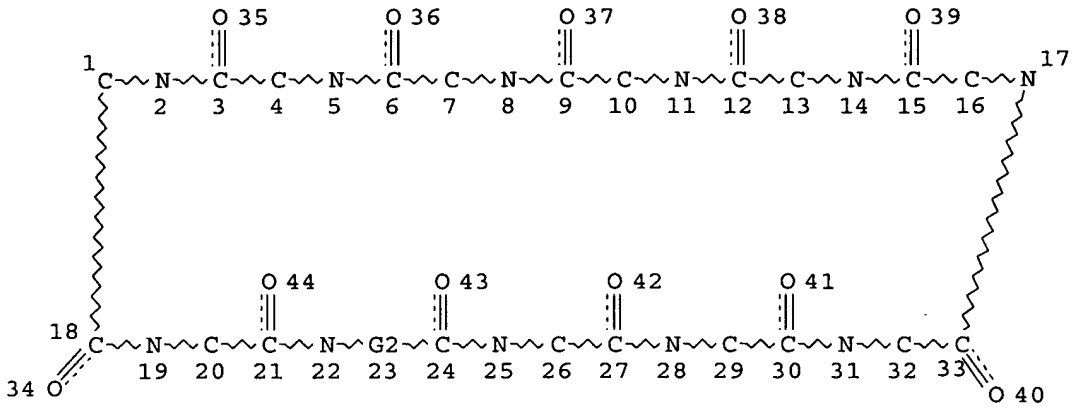
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 49

STEREO ATTRIBUTES: NONE
L2 STR



CH^CH3 CH2·CH2·CH2
@45 46 @47 48 @49

VAR G2=45/47-22 49-24
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 49

STEREO ATTRIBUTES: NONE
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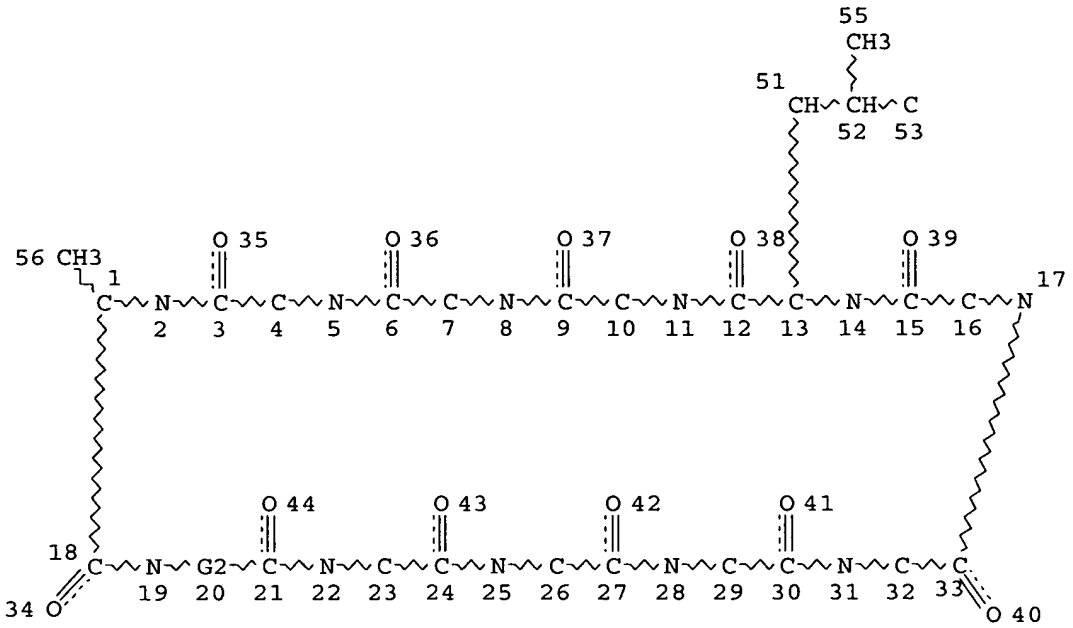

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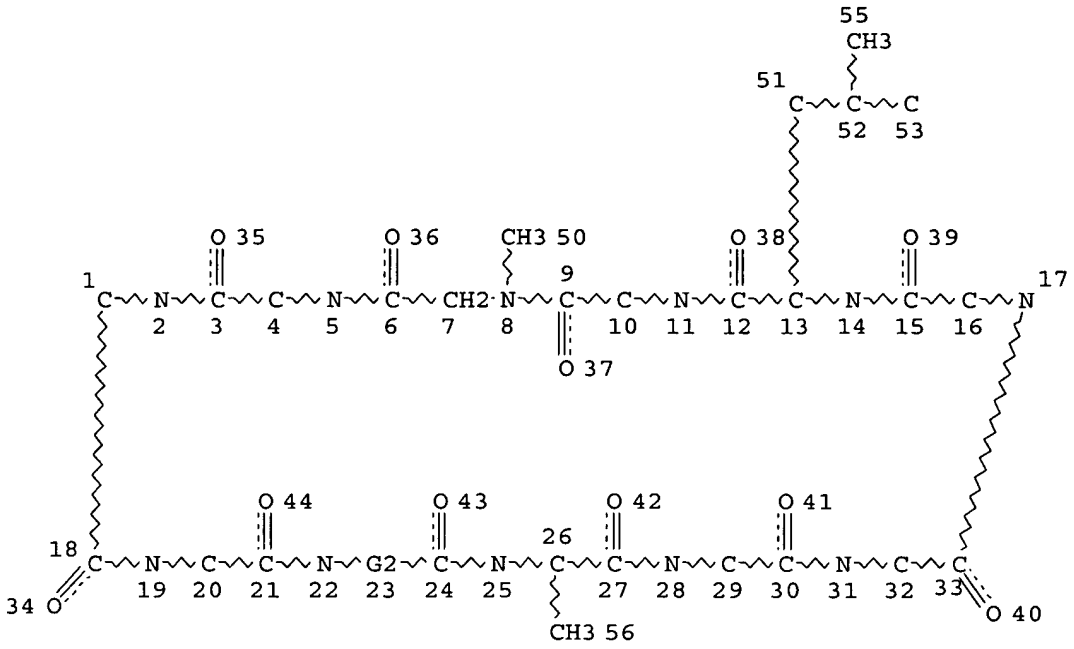
VAR G2=45/47-19 49-21
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 54

STEREO ATTRIBUTES: NONE
L22 STR



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VAR G2=45/47-22 49-24
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 55

STEREO ATTRIBUTES: NONE
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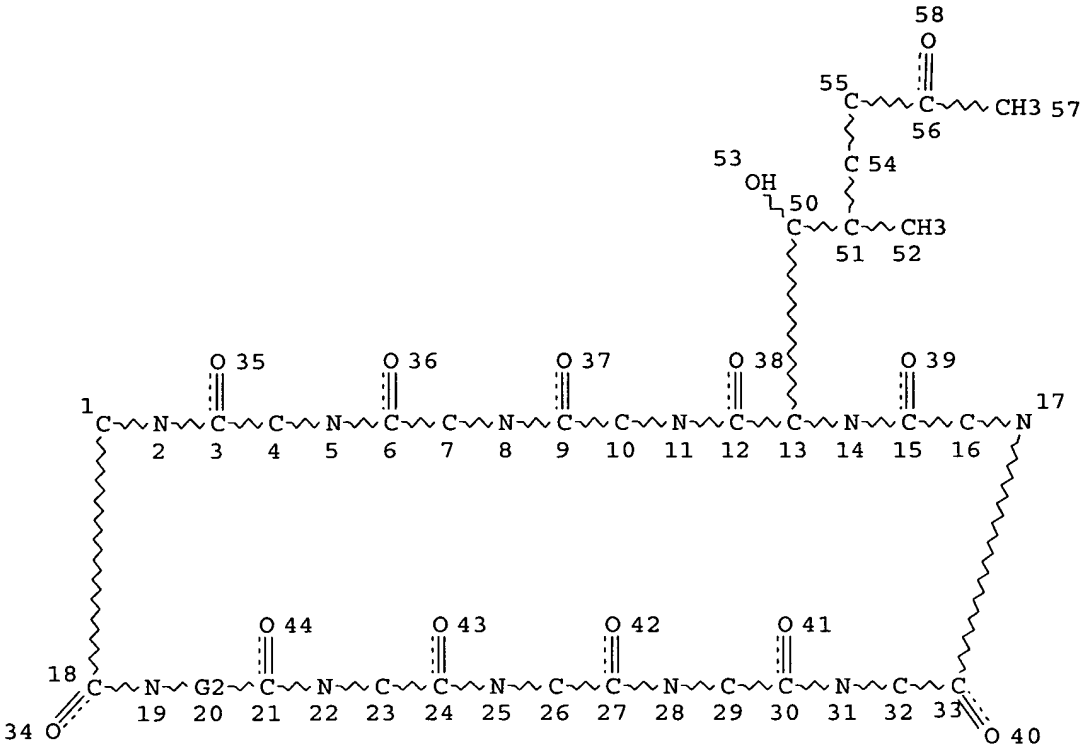

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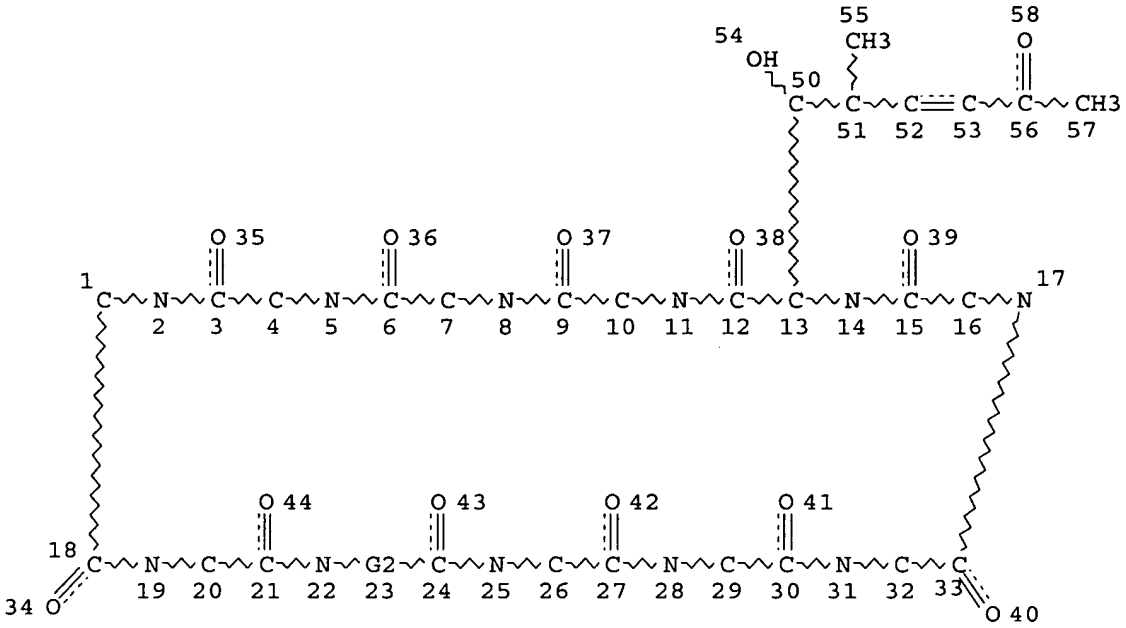
Page 2-A
VAR G2=45/47-19 49-21
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 58

STEREO ATTRIBUTES: NONE
L29 STR



VAR G2=45/47-22 49-24
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 58

STEREO ATTRIBUTES: NONE

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L46	21	SEA FILE=HCAPLUS ABB=ON PLU=ON ("HAYDAR S"/AU OR "HAYDAR S N"/AU) OR "HAYDAR SIMON"/AU OR "HAYDAR SIMON N"/AU
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L52	1	SEA FILE=HCAPLUS ABB=ON PLU=ON L50 AND L51
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L56 ANSWER 1 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:248290 HCAPLUS
TITLE: Substituted 3-arylsulfonyl-7-azaindoles as novel 5-HT6 agonists
AUTHOR(S): McDevitt, Robert E.; Antane, Schuyler A.; Beyer, Chad E.; Chen, Ping; Gross, Jonathan L.; **Haydar, Simon N.**; Hughes, Zoe. A.; Le, Van-Duc; Mabrouk, Omar; Malberg, Jessica E.; Robichaud, Albert J.; Shenoy, Rajesh A.; Smith, Deborah L.; Wang, Xintao G.; Zhang, Guo Ming; Schechter, Lee. E.
CORPORATE SOURCE: Department of Medicinal Chemistry, Chemical and Screening Sciences, Wyeth Research, Princeton, NJ, 08543, USA
SOURCE: Abstracts of Papers, 231st ACS National Meeting, Atlanta, GA, United States, March 26-30, 2006 (2006), MEDI-137. American Chemical Society: Washington, D. C.
CODEN: 69HYEC
DOCUMENT TYPE: Conference; Meeting Abstract; (computer optical disk)
LANGUAGE: English
AB In recent years much investigation has been focused on higher-order serotonin receptors in the hopes of elucidating their functional roles. 5-HT6 receptors are exclusively localized within the CNS and pos. coupled to an adenylate cyclase second messenger system. The ability of 5-HT6 receptors to regulate neurotransmitter release has further demonstrated the potential for this receptor in the treatment of a number of disease targets such as cognition, anxiety and depression. Our earlier work identified novel 3-Arylsulfonyl-7-Azaindoles as potent ligands of 5-HT6 receptors. Herein we describe the synthesis and effects of substitutions on the 7-Azaindole core. Select examples within this series were revealed to be full 5-HT6 agonists based on cAMP accumulation studies and were shown to be active in a rat behavioral model of anxiety.

L56 ANSWER 2 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:248289 HCAPLUS
TITLE: 1-(2-Aminoethyl)-3-(arylsulfonyl)-1-H-7-azaindoles as Novel 5-HT6 receptor ligands
AUTHOR(S): **Haydar, Simon N.**; Antane, Schuyler; Ping, Chen; Gross, Jonathan L.; McDevitt, Bob; Le, Van-Duc; Malberg, Jessica; Robichaud, Albert J.; Shenoy, Rajesh A.; Smith, Deborah L.; Zhang, Guo Ming; Schechter, Lee E.
CORPORATE SOURCE: Department of Medicinal Chemistry, Chemical and Screening Sciences, Wyeth Research, Princeton, NJ, 08543, USA
SOURCE: Abstracts of Papers, 231st ACS National Meeting, Atlanta, GA, United States, March 26-30, 2006 (2006), MEDI-136. American Chemical Society: Washington, D. C.
CODEN: 69HYEC
DOCUMENT TYPE: Conference; Meeting Abstract; (computer optical disk)
LANGUAGE: English
AB The 5-HT6 receptor is one of the latest G-protein coupled receptors (GPCR)

to have been identified in the serotonin family. The central nervous system (CNS) localization of the 5-HT6 receptors and their affinity for CNS drugs have created intense interest in identifying selective 5-HT6 receptors modulators as tools for studying the receptor and its' potential therapeutic applications. Novel 1-(aminoethyl)-3-(arylsulfonyl)1-H-7-azaindoles were prepared and several analogs within this class have been identified as high-affinity 5-HT6 receptor ligands functioning as full agonists. The synthesis and structure activity relationship of this potent class will be discussed.

L56 ANSWER 3 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:167849 HCAPLUS
TITLE: Aryl- and heteroaryl-substituted tetrahydroisoquinolines and their preparation, pharmaceutical compositions and use thereof to block reuptake of norepinephrine, dopamine, and serotonin for the treatment of neurological and psychological disorders
INVENTOR(S): **Molino, Bruce F.**; Liu, Shuang; Berkowitz, Barry A.; Guzzo, Peter R.; Beck, James P.; Cohen, Marlene
PATENT ASSIGNEE(S): Amr Technology, Inc., USA; Bristol-Myers Squibb Company
SOURCE: PCT Int. Appl., 570 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006020049	A2	20060223	WO 2005-US25193	20050715
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006052378	A1	20060309	US 2005-183066	20050715
PRIORITY APPLN. INFO.:			US 2004-588448P	P 20040715

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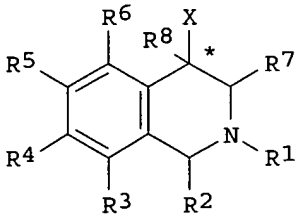

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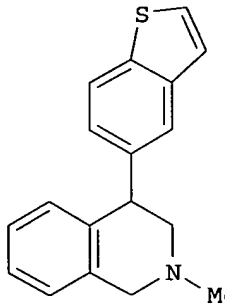

II

AB This invention dicloses the preparation of compds. of formula I and their pharmaceutical composition and use for norepinephrine, dopamine, and serotonin reuptake inhibition to treat neurol. and psychol. disorders and their use in combination therapy. Compds. of formula I wherein * is in the (R) or (S) configuration; X is (un)substituted fused bicyclic carbocycle or heterocycle; R1 and R7 are independently H, (un)substituted C1-6 alkyl, (un)substituted C2-6 alkenyl, (un)substituted C2-6 alkynyl, (un)substituted C3-6 cycloalkyl, or (un)substituted C4-7 cycloalkylalkyl; R2 is H, (un)substituted C1-6 (halo)alkyl, (un)substituted C2-6 alkenyl, (un)substituted C2-6 alkynyl, (un)substituted C3-6 cyclalkyl, or (un)substituted C4-7 cycloalkylalkyl; R3, R4, R5, and R6 are independently H, halo, OH and derivs., S(O)nH and derivs. CN, C(O)H and derivs., CONH2 and derivs., NH2 and derivs., (un)substituted C1-6 alkyl, (un)substituted C2-6 alkenyl, (un)substituted C2-6 alkynyl, (un)substituted C3-6 cycloalkyl, or (un)substituted C4-7 cycloalkylalkyl; R8 is H, halo, OH and derivs., SH and derivs. C1-6 alkyl, CN, or NH2 and derivs.; n is 0,1, or 2; and pharmaceutically acceptable salts and oxides thereof are claimed in this invention. Example compds. (+)- and (-)-II.HCl was prepared by S-alkylation of 4-bromobenzenethiol with bromoacetaldehyde di-Et acetal and the resulting (4-bromophenylsulfanyl)acetaldehyde di-Et acetal underwent cyclization to give 5-bromobenzothiophene that underwent Suzuki coupling with 4-isoquinolinylboronic acid to give 4-(5-benzothienyl)isoquinoline, which was N-methylated and the resulting methylated isoquinoline underwent reduction to give tetrahydroisoquinoline derivative that was separated by chiral HPLC to give optically enriched (+)- and (-)-II, which was treated with HCl to give (+)- and (-)-II.HCl. Addnl. 153 example compds. were prepared using similar procedures. All the invention compds. were evaluated for their ability to block reuptake of norepinephrine, dopamine and serotonin. The functional ability of the invention compds. to inhibit neurotransmitter uptake was established by measuring the inhibition of [3H]-noradrenaline, [3H]-serotonin, and [3H]-dopamine uptake into the rat brain synaptosomes. From the inhibition of radioligand binding at the human biogenic amine transporter assays. it was determined that the invention compds. are potent inhibitors of monamine reuptake by the dopamine (DAT) norepinephrine (NET) and serotonin (SET) transporters. Compound (+)-II.HCl showed binding affinities (Ki values) of 1.2%, 3.8%, 4.0% inhibition of NET, DAT and SERT resp. at 100 nM concentration

L56 ANSWER 4 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:120480 HCAPLUS
DOCUMENT NUMBER: 144:192506
TITLE: Novel processes for stereoselective synthesis of trans ISATX247
INVENTOR(S): **Molino, Bruce F.; Yang, Zhicai;**

Maeng, Jun-Ho; Manning, David D.
PATENT ASSIGNEE(S): Amr Technology, Inc., USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006014872	A2	20060209	WO 2005-US26319	20050726

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-592330P P 20040729

AB The invention relates to a process for preparation of trans ISATX247 and deuterated derivs. cyclo(A-Abu-Sar-MeLeu-Val-MeLeu-Ala-D-Ala-MeLeu-MeLeu-MeVal) [A = -NMeCH[CH(OH)CHMeCH2CH:CHCR3:CR1R2]CO-; stereo αS,βR,γR,E] (R1, R2, R3 = H or D) by application of organozirconium chemical The process involves reacting an acetyl **cyclosporin** aldehyde with an organozirconium reagent to provide acetyl **cyclosporin** diene (the acetate of trans ISATX247) and deacetylating the acetyl **cyclosporin** diene to produce the trans-isomer of ISATX247. The invention also relates to a process for preparing the same trans ISATX247 compound by olefin cross metathesis of acetyl **cyclosporin** A to afford acetyl **cyclosporin** α,β-unsatd. aldehyde, followed by Wittig reaction and deacetylation. Also disclosed are processes for preparing an acetyl **cyclosporin** α,β-unsatd. aldehyde compound and a **cyclosporin** triene analog compound Thus, trans ISATX247 acetate was prepared in 47% yield by treating acetyl **cyclosporin** aldehyde with propargyltrimethylsilane, Cp2Zr(H)Cl, and AgClO4 in CH2Cl2.

L56 ANSWER 5 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:739631 HCAPLUS
TITLE: 1-(2-Aminoethyl)-3-(arylsulfonyl)-1H-pyrrolopyridines as novel 5-HT6 receptor ligands
AUTHOR(S): Bernotas, Ronald C.; Antane, Schuyler A.; Lenicek, Steven; **Haydar, Simon N.**; Robichaud, Albert J.; Zhang, Guo Ming; Smith, Deborah L.; Coupet, Joseph; Schechter, Lee E.
CORPORATE SOURCE: Chemical and Screening Sciences, Wyeth Research, Collegeville, PA, 19426, USA
SOURCE: Abstracts of Papers, 230th ACS National Meeting, Washington, DC, United States, Aug. 28-Sept. 1, 2005 (2005), MEDI-117. American Chemical Society: Washington, D. C.
CODEN: 69HFCL
DOCUMENT TYPE: Conference; Meeting Abstract; (computer optical disk)
LANGUAGE: English

AB We have demonstrated that many 1-(2-aminoethyl)-3-arylsulfonyl-1H-indoles 2 are 5-HT6 ligands. Introduction of an addnl. nitrogen in the indole ring provided 1-(2-aminoethyl)-3-arylsulfonyl-1H-pyrrolo1;2,3-b3;pyridines 3, which proved to have generally higher 5-HT6 affinity compared to 2. Appropriate substitution on 3 led to full agonists or full antagonists in a 5-HT6 functional (cyclase) assay. We report here the synthesis of the three regioisomeric pyrrolopyridines (4, 5, and 6) by several routes and describe their 5-HT6 binding and functional activity.

L56 ANSWER 6 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:177896 HCAPLUS
DOCUMENT NUMBER: 142:280225
TITLE: Preparation of capped aminopyrazinoylguanidines as sodium channel blockers
INVENTOR(S): Johnson, Michael R.; **Molino, Bruce F.**; Zhang, Jianzhong; Sargent, Bruce J.
PATENT ASSIGNEE(S): Parion Sciences, Inc., USA
SOURCE: PCT Int. Appl., 100 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005018644	A1	20050303	WO 2004-US26885	20040818
WO 2005018644	B1	20050512		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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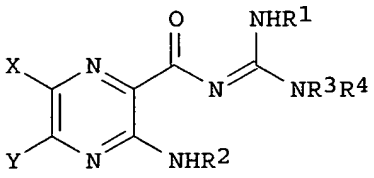
US 2005080091	A1	20050414	US 2004-920410	20040818
US 2005234072	A1	20051020	US 2005-131262	20050518
US 2005228182	A1	20051013	US 2005-138280	20050527
US 2006052394	A1	20060309	US 2005-211422	20050826
US 2006052395	A1	20060309	US 2005-211660	20050826

PRIORITY APPLN. INFO.: US 2003-495725P P 20030818
US 2004-920410 A1 20040818

OTHER SOURCE(S): MARPAT 142:280225
GI



I

AB Title compds. [I; X = H, halo, CF3, alkyl, (substituted) Ph, etc.; Y = H,

OH, SH, alkoxy, alkylthio, halo, alkyl, (substituted) aryl, etc.; R1 = H, alkyl; R2 = R7, (CH2)mOR8, (CH2)mNR7R10, (CH2CH2O)mR8, etc.; m = 1-7; R3, R4 = H, alkyl, hydroxyalkyl, Ph, phenylalkyl, naphthylalkyl, pyridylalkyl, etc.; R7 = H, alkyl, (substituted) Ph, etc.; R8 = H, alkyl, 2-tetrahydropyranyl, glucuronide, etc.; R10 = H, SO2Me, COR13, CO2R13, etc.; R13 = H, R7, R10, etc.; with provisos], were prepared Thus, [4-(4-hydroxyphenyl)butyl]carbamic acid benzyl ester in EtOH at 70° was treated with oxiranylmethanol over 4 h to give 4.6% [4-[4-[3-(2,3-dihydroxypropoxy)-2-hydroxypropoxy]phenyl]butyl]carbamic acid benzyl ester. This was hydrogenolyzed in EtOH over Pd/C to give 51% 3-[3-[4-(4-aminobutyl)phenoxy]-2-hydroxypropoxy]propane-1,2-diol. The latter was stirred with Et3N and 1-(3,5-diamino-6-chloropyrazine-2-carbonyl)-2-methylisothiourea hydroiodide in EtOH at 65° to give 36% N-(3,5-diamino-6-chloropyrazine-2-carbonyl)-N'-[4-[4-[3-(2,3-dihydroxypropoxy)-2-hydroxypropoxy]phenyl]butyl]guanidine (PSA 15143). The latter showed Na channel blocking activity with EC50 = 7 nM.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 7 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:934323 HCAPLUS
DOCUMENT NUMBER: 141:395708
TITLE: Substituted heterocycle fused gamma-carbolines
INVENTOR(S): Robichaud, Albert J.; Lee, Taekyu; Deng, Wei; Mitchell, Ian S.; Yang, Michael G.; **Haydar, Simon**; Chen, Wenting; McClung, Christopher D.; Calvello, Emilie J.; Zawrotny, David M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 150 pp., Cont.-in-part of U.S. Ser. No. 370,878.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2004220178	A1	20041104	US 2004-787941		20040226
US 6552017	B1	20030422	US 2000-595250		20000615
US 2004034015	A1	20040219	US 2003-370878		20030220
PRIORITY APPLN. INFO.:			US 1999-139321P	P	19990615
			US 2000-595250	A3	20000615
			US 2003-370878	B2	20030220

OTHER SOURCE(S): MARPAT 141:395708
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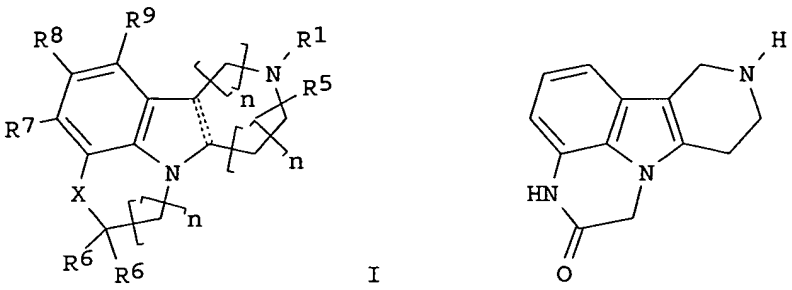
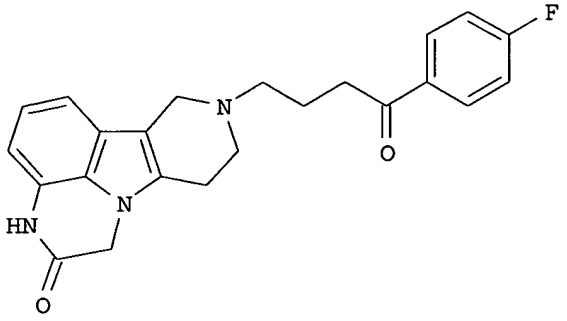


I

II



III

AB The preparation of compds., I (R 1 = H, ketone, ester, alkyl, alkene, cycloalkyl, aryl; R 5 = H, C1-4 alkyl; R6 = H, OH, alkylamine, CF3, C1-4 alkyl, C2-4 alkenyl, C2-4 alkynyl. C1-4 alkoxy, C1-4 haloalkyl, C3-6 cycloalkyl, aryl; R7, R8, R9 = H, halo, CF3, OCF3, OH, CN, NO2, amine, alkyl, alkenyl etc.; X = NH or substituted amine; dashed line = single or double bond ; n = independently integers form 0-3) as serotonin 5-HT2 agonists and antagonist for the treatment of addictive behavior and sleep disorders is described. Thus, II was dissolved in Me Et ketone and treated with KI, K2CO3, and 4-chloro-4'-fluorobutyrophenone to give the target compound III.

L56 ANSWER 8 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:757872 HCAPLUS
DOCUMENT NUMBER: 139:276893
TITLE: Preparation of azabenzothiopyranoindazoles with antitumor activity
INVENTOR(S): **Haydar, Simon N.**
PATENT ASSIGNEE(S): Albany Molecular Research, Inc., USA
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

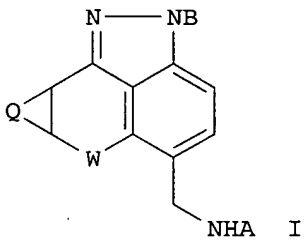
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003078647	A2	20030925	WO 2003-US7582	20030311
WO 2003078647	A3	20040408		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,

TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003225069	A1	20031204	US 2002-96421	20020312
US 6747039	B2	20040608		

PRIORITY APPLN. INFO.: US 2002-96421 A 20020312
OTHER SOURCE(S): MARPAT 139:276893
GI



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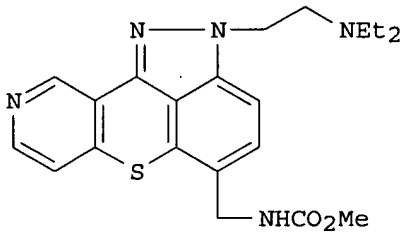


II

AB Title compds. [I; W = S, SO, SO2; Q = 5- or 6-membered aromatic ring having ≥1 N, S; A = H, (substituted) (cyclic) alkyl, alkoxy, OH, CHO, CO2R1, SO2R1, (CH2)nNH(CH2)mMe, (CH2)nN[(CH2)mMe](CH2)pMe, (CH2)nD; B = H, (substituted) (cyclic) alkyl, alkoxy, OH, (CH2)nNH(CH2)mMe; (CH2)nN[(CH2)mCH3](CH2)pMe, (CH2)nD; R1 = alkyl, Ph, phenylalkyl; n = 2-3; m, p = 0-3; D = OH, (substituted) alkoxy, 5-6 membered (aromatic) heterocyclyl containing S, O, or N], were prepared Thus, title compound (II) (multistep preparation from 3-chlorothiophenol, 4-chloronicotinic acid, and H2NNHCH2CH2NEt2 given) showed GI50 = 0.1 μM against HeLa S-3 cells.

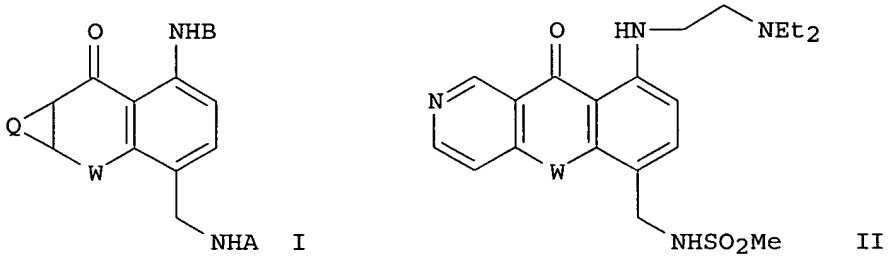
L56 ANSWER 9 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:757871 HCAPLUS
DOCUMENT NUMBER: 139:276881
TITLE: Preparation of azathioxanthenones with antitumor activity
INVENTOR(S): **Haydar, Simon N.**
PATENT ASSIGNEE(S): Albany Molecular Research, Inc., USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003078646	A2	20030925	WO 2003-US7581	20030311
WO 2003078646	A3	20040304		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,

FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003212061 A1 20031113 US 2002-96420 20020312
PRIORITY APPLN. INFO.: US 2002-96420 A 20020312
OTHER SOURCE(S): MARPAT 139:276881
GI



AB Title compds. [I; W = S, SO, and SO2; Q = atoms to form a 5- or 6-membered aromatic ring having ≥1 N, S; A = H, (cyclic) (substituted) alkyl, alkoxy, OH, CHO, CO2R1, SO2R1, (CH2)nNH(CH2)mMe, (CH2)nN[(CH2)mCH3](CH2)pMe, (CH2)nD; B = H, (cyclic) (substituted) alkyl, alkoxy, OH, (CH2)nNH(CH2)mMe, (CH2)nN[(CH2)mCH3](CH2)pMe, (CH2)nD; R1 = alkyl, Ph, phenylalkyl; n = 2-3; m, p = 0-3; D = OH, (substituted) alkoxy, 5-6 member (aromatic) heterocyclyl containing S, O, or N], were prepared Thus, title compound (II; W = S) (multistep preparation from 3-chlorothiophenol and 4-chloronicotinic acid given) inhibited HeLa cells with GI50 = 0.4 μM.

L56 ANSWER 10 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:753467 HCAPLUS
DOCUMENT NUMBER: 139:250903
TITLE: Investigation of Oxygen Interaction with a Pt-Rh/Al2O3 Catalyst by a Differential Temperature-Programmed Desorption Method
AUTHOR(S): Lecomte, J. J.; **Haydar, S.**; Granger, P.; Leclercq, L.; Leclercq, G.; Joly, J. P.
CORPORATE SOURCE: Laboratoire d'Application de la Chimie a l'Environnement, Universite Claude Bernard Lyon 1, Villeurbanne, 69622, Fr.
SOURCE: Langmuir (2003), 19(22), 9266-9270
CODEN: LANGD5; ISSN: 0743-7463
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The interaction between gaseous oxygen and a catalyst Pt-Rh supported on γ-Al2O3 (sp. surface area: 100 m2 g-1) was investigated by means of a differential desorption technique called intermittent temperature-programmed desorption (ITPD). Expts. were carried out under conventional secondary vacuum (P ≈ 10-4 Pa). Essentially, three desorption steps α, β1, and β2 were observed, occurring around 350, 650, and 750 K, resp. Steps β1 and β2 stem from the desorption of oxygen strongly and dissociatively adsorbed on the metallic particles. Desorption step α is better observed after oxygen adsorption at ambient temperature; it corresponds to weakly bonded oxygen. The high values of the frequency factors strongly suggest that no readsorption occurred when oxygen desorbed through steps β1 and β2. Desorption activation

energies for steps β1 and β2 were estimated at 219 and 305 kJ/mol, resp.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 11 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:630052 HCAPLUS
TITLE: Chemo-enzymatic modification of immunosuppressant **cyclosporin** A
AUTHOR(S): Hemenway, Michael H.; Zhang, Qibo; Michels, Peter C.; **Rich, Joseph O.**; Khmelnitsky, Yuri L.; **Haydar, Simon N.**; **Molino, Bruce F.**
CORPORATE SOURCE: Albany Molecular Research, Inc, Mount Prospect, IL, 60056, USA
SOURCE: Abstracts of Papers, 226th ACS National Meeting, New York, NY, United States, September 7-11, 2003 (2003), BIOL-185. American Chemical Society: Washington, D. C.
CODEN: 69EKY9
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB **Cyclosporin** A is the most widely prescribed drug for rejection suppression after organ transplantation. However, chronic use of this agent can lead to loss of the transplanted organ due to its nephrotoxicity and neurotoxicity. Decades of investigation have led to the syntheses of more than 3000 **cyclosporin** analogs, but thus far no improved **cyclosporin** analogs has made it to the market. Here we report a chemo-enzymic approach for efficient generation of novel **cyclosporin** A derivs.

L56 ANSWER 12 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:432173 HCAPLUS
TITLE: Biaryl purine derivatives as potent inhibitors of cyclin-E/CDK2, cell growth, and cell cycle progression
AUTHOR(S): Trova, Michael P.; Friedrich, Thomas D.; Alicea, L. R.; Barford, C. A.; Barnes, K. D.; Benanti, T.; Bergeron, M. E.; Bielaska, M.; Bilotta, J. A.; Burry, L. C.; Davisdon, M. R.; Duong, T. N.; **Haydar, S. N.**; Hui, Y.; Johnson, M. R.; Johnson, R. E.; Lu, J.; Murphy, C. M.; O'Grady, H. R.; Peace, D.; Rainka, M. P.; Russell, M.; Salamone, S.; Smith, J. L.; Snider, P. A.; Toporowski, J. W.; Tregay, S. W.; Wilson, A. C.; Wyle, M. J.; Yao, X.; Zheng, X.
CORPORATE SOURCE: Albany Molecular Research, Inc., Albany, NY, USA
SOURCE: Abstracts, 31st Northeast Regional Meeting of the American Chemical Society, Saratoga Springs, NY, United States, June 15-18 (2003), 58. American Chemical Society: Washington, D. C.
CODEN: 69EBFV
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB A novel series of purine derivs., containing a 6-[(biarylmethyl)amino] substituent, was prepared The compds. were evaluated in vitro as cyclin/CDK inhibitors and as cell growth inhibitors. We will present the syntheses and structure activity relationships (SARs) of this novel series of analogs. We will also describe some biochem. studies designed to elucidate the effects of these compds. on cell culture. It is expected that compds. with these in vitro and cellular activities may be useful as antitumor agents.

L56 ANSWER 13 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:103597 HCAPLUS
DOCUMENT NUMBER: 139:182281
TITLE: Adsorption of p-nitrophenol on an activated carbon with different oxidations
AUTHOR(S): **Haydar, S.**; Ferro-Garcia, M. A.; Rivera-Utrilla, J.; Joly, J. P.
CORPORATE SOURCE: Laboratoire d'Application de la Chimie a l'Environnement, UMR 5634 CNRS-Universite Claude Bernard Lyon 1, Villeurbanne, 69622, Fr.
SOURCE: Carbon (2003), 41(3), 387-395
CODEN: CRBNAH; ISSN: 0008-6223
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An activated carbon prepared from olive stones has been modified through oxidation by nitric acid or sodium hypochlorite. These treatments introduced large amts. of oxygen groups, which were characterized by mass-spectrometry and temperature-programmed desorption. Both CO2- and CO-evolving groups were created by these oxidation treatments. A portion of these oxidized specimens was then outgassed under vacuum at ≤823 K to remove most of the CO2-evolving groups from their surface. Oxidized specimens have a smaller surface area than that of the original specimen. Subsequent partial outgassing increases the surface area which, however, does not reach the value it had before oxidation p-Nitrophenol (PNP) adsorption isotherms from aqueous solns. were determined at 298 K for the original, oxidized, and partly outgassed specimens. The results confirm an intermediate plateau at low equilibrium PNP concentration at .apprx.10 mg/L. The relative effects of textural vs. surface chemical on PNP uptake are then discussed. CO-evolving groups had no influence on PNP uptake. The models in which carbonylic groups are basic adsorption sites for substituted phenols can be ruled out for the entire isotherm of PNP obtained with the original carbon. These models are also unlikely for PNP adsorption on oxidized and partly outgassed specimens.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 14 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:636233 HCAPLUS
DOCUMENT NUMBER: 138:66809
TITLE: Risk-directed immunosuppression in heart transplant recipients: maintenance prednisone can be avoided in selected patients
AUTHOR(S): Arnold, A. N.; Huffman, M.; Eich, D. M.; Bernstein, R. C.; Old, W. D.; Mooney, M.; Szentpetery, S.; Hagberg, R.; McGrath, M.; **Rich, J.**; Herre, J. M.; Barnhart, G. R.
CORPORATE SOURCE: Heart Transplant Program, Sentara Norfolk General Hospital, Norfolk, VA, USA
SOURCE: Transplantation Proceedings (2002), 34(5), 1830-1833
CODEN: TRPPA8; ISSN: 0041-1345
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Patients who received orthotrophic heart transplantation from 1994 to 1998 were studied retrospectively to determine if risk-directed immunosuppression results in good outcome, as measured by patient survival and time to rejection. The study clearly demonstrated that a risk-directed anal. can

select patients for double-drug immunosuppression without maintenance steroids. These selected patients experience severe rejection less frequently and have a patient survival that is similar to patients given triple-drug immunosuppression. The results are obtained without the need for more calcineurin inhibitor or antimetabolite. The improved freedom from severe rejection validates this prospective approach to the selection of a group of patients at lower risk for severe rejection.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 15 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:136720 HCAPLUS
DOCUMENT NUMBER: 136:401897
TITLE: Recent syntheses of epibatidine. A review
AUTHOR(S): Olivo, Horacio F.; **Hemenway, Michael S.**
CORPORATE SOURCE: Division of Medicinal and Natural Products Chemistry, College of Pharmacy, The University of Iowa, Iowa City, IA, 52242, USA
SOURCE: Organic Preparations and Procedures International (2002), 34(1), 1-26
CODEN: OPPIAK; ISSN: 0030-4948
PUBLISHER: Organic Preparations and Procedures, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. The syntheses of epibatidine via cycloaddn. reactions, intramol. nucleophilic displacement reactions and radical cyclizations are discussed.
REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 16 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:779595 HCAPLUS
DOCUMENT NUMBER: 136:183752
TITLE: Synthesis of regioisomeric 2,5-bis-substituted-aza-benzothiopyranoindazoles
AUTHOR(S): Krapcho, A. Paul; **Haydar, Simon N.**
CORPORATE SOURCE: Department of Chemistry, The University of Vermont, Burlington, VT, 05405, USA
SOURCE: Journal of Heterocyclic Chemistry (2001), 38(5), 1153-1166
CODEN: JHTCAD; ISSN: 0022-152X
PUBLISHER: HeteroCorporation
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:183752
AB The synthesis of 6-chloro-9-nitro-benzothiopyranopyridin-5-ones (I) has been accomplished. The [3,2-c] analog could not be prepared since attempts to cyclize 3-(2-nitro-5-chlorophenoxy)pyridine-2-carboxylic acid led to the decarboxylation product 3-(2-nitro-5-chlorothiophenoxy) pyridine (40). Treatment of I with substituted hydrazines led to 2-(substituted)-5-nitropyridothiopyranoindazoles. The reduction of the nitro groups of these substrates was effected by treatment with hydrogen gas (palladium catalyst) or by stannous chloride to yield the 5-amino analogs. The conversion of these derivs. to the 2,5-bis(alkylamino)-7-, 8- and 9-aza benzothiopyranoindazoles was accomplished by direct alkylations, acylations, followed by reduction of the amido group with Red-Al or lithium aluminum hydride, or by reductive alkylations in the presence of sodium cyanoborohydride. The removal of the protective BOC-group was effected by treatment of the appropriate substrates with anhydrous hydrogen chloride.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 17 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:455255 HCAPLUS
DOCUMENT NUMBER: 135:195401
TITLE: A regiospecific synthesis of 3,3,6-trimethylindan-1-one
AUTHOR(S): Vogt, Paul F.; **Molino, Bruce F.**; Robichaud, Albert J.
CORPORATE SOURCE: Department of Medicinal Chemistry, Albany Molecular Research, Inc., Albany, NY, 12203, USA
SOURCE: Synthetic Communications (2001), 31(5), 679-684
CODEN: SYNCAV; ISSN: 0039-7911
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:195401
AB A novel, regiospecific synthesis of 3,3,6-trimethylindan-1-one (I) was achieved. The route to I was 6 steps and proceeded in 27% overall yield.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 18 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:390929 HCAPLUS
DOCUMENT NUMBER: 135:65844
TITLE: Sediment discharges in river beds: a potential contribution to environmental standards
AUTHOR(S): **Molino, B.**; Masi, G.
CORPORATE SOURCE: Dipartimento di Ingegneria e Fisica dell'Ambiente, Universita degli Studi della Basilicata, Romana, 85100, Italy
SOURCE: Ingegneria Ambientale (2000), 29(3/4), 143-148
CODEN: IGEABH; ISSN: 0394-5871
PUBLISHER: C.I.P.A. Srl
DOCUMENT TYPE: Journal
LANGUAGE: Italian
AB This paper originates from environmental Italian laws anal. relating to the discharge in stream. The laws concern particularly the suspended solid concentration parameter. This also is compared with the same parameter values in International Laws. The Camastra stream (Southern Italy) is monitored by a series of water sampling in different sections and particularly in the river bed downstream from Ponte Fontanelle reservoir to its confluence with the Basento River. The suspended solid concentration during water discharge is monitored.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 19 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:324974 HCAPLUS
DOCUMENT NUMBER: 135:61467
TITLE: Microbial hydroxylation of nitrogen-substituted azabicycloalkanes and its application to a total synthesis of epibatidine
AUTHOR(S): **Hemenway, Michael Scott**
CORPORATE SOURCE: Univ. of Iowa, Iowa City, IA, USA
SOURCE: (2000) 224 pp. Avail.: UMI, Order No. DA9975820 From: Diss. Abstr. Int., B 2000, 61(6), 3019
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L56 ANSWER 20 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:900647 HCAPLUS
DOCUMENT NUMBER: 134:56657
TITLE: Preparation of substituted heterocycle fused gamma-carbolines
INVENTOR(S): Robichaud, Albert J.; Lee, Taekyu; Deng, Wei; Mitchell, Ian S.; **Haydar, Simon**; Chen, Wenting; McClung, Christopher D.; Calvello, Emilie J. B.; Zawrotny, David M.
PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 764 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077010	A2	20001221	WO 2000-US16373	20000615
WO 2000077010	A3	20010628		
W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2373920	AA	20001221	CA 2000-2373920	20000615
EP 1192165	A2	20020403	EP 2000-942807	20000615
EP 1192165	B1	20040922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000012411	A	20020416	BR 2000-12411	20000615
TR 200103658	T2	20020621	TR 2001-200103658	20000615
JP 2003502336	T2	20030121	JP 2001-503867	20000615
US 6713471	B1	20040330	US 2000-594954	20000615
AT 277055	E	20041015	AT 2000-942807	20000615
ES 2223536	T3	20050301	ES 2000-942807	20000615
ES 2223537	T3	20050301	ES 2000-942808	20000615
ES 2228549	T3	20050416	ES 2000-941453	20000615
ZA 2001009735	A	20040127	ZA 2001-9735	20011127
NO 2001006128	A	20020211	NO 2001-6128	20011214
PRIORITY APPLN. INFO.:			US 1999-139321P P	19990615
			WO 2000-US16373 W	20000615

OTHER SOURCE(S): MARPAT 134:56657
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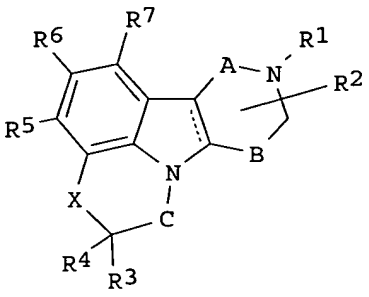

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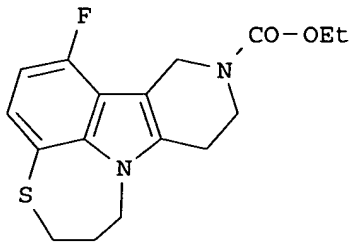


II

AB Novel γ-carboline compds. of formula I [R1, R2 = H, acyl, alkyl, cycloalkyl, etc.; R3, R4 = H, OH, amino, CF3, alkyl, etc.; R5-R7 = H, halo, CF3, OH, CN, alkyl, aryl, heterocycle, etc.; X = (substituted) NH, (substituted) CONH, (substituted) NHCO, S; A, B, C = (CH2)n, n = 0-3] are prepared The invention is also concerned with pharmaceutical formulations comprising these novel compds. as active ingredients and the use of the novel compds. and their formulations in the treatment of certain disorders. The compds. of this invention are serotonin agonists and antagonists and are useful in the control or prevention of central nervous system disorders including obesity, anxiety, depression, psychosis, schizophrenia, sleep disorders, sexual disorders, migraine, conditions associated with cephalic pain, social phobias, and gastrointestinal disorders such as dysfunction of the gastrointestinal tract motility. Thus, II is prepared starting from p-fluorophenol, β-propiolactone and 1-carbethoxy-4-piperidone. Pharmaceutical compns. containing I are described.

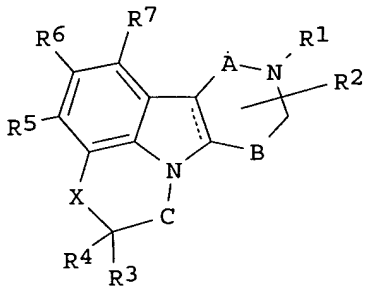
L56 ANSWER 21 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:900639 HCAPLUS
DOCUMENT NUMBER: 134:56655
TITLE: Preparation of substituted heterocycle fused gamma-carbolines
INVENTOR(S): Robichaud, Albert J.; Lee, Taekyu; Deng, Wei; Mitchell, Ian S.; Yang, Michael Guang; **Haydar, Simon**; Chen, Wenting; McClung, Christopher D.; Calvello, Emilie J. B.; Zawrotny, David M.
PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 308 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077002	A1	20001221	WO 2000-US16498	20000615
W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2374239	AA	20001221	CA 2000-2374239	20000615
EP 1189904	A1	20020327	EP 2000-941453	20000615
EP 1189904	B1	20040922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

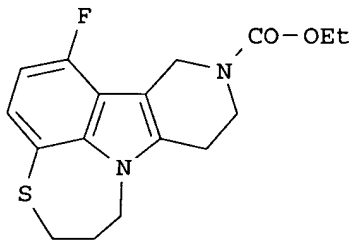
BR 2000012086	A	20020402	BR 2000-12086		20000615
TR 200103658	T2	20020621	TR 2001-200103658		20000615
JP 2003502331	T2	20030121	JP 2001-503860		20000615
NZ 516031	A	20031031	NZ 2000-516031		20000615
US 6713471	B1	20040330	US 2000-594954		20000615
AT 277048	E	20041015	AT 2000-941453		20000615
ES 2223536	T3	20050301	ES 2000-942807		20000615
ES 2223537	T3	20050301	ES 2000-942808		20000615
ES 2228549	T3	20050416	ES 2000-941453		20000615
ZA 2001009735	A	20040127	ZA 2001-9735		20011127
NO 2001006116	A	20020211	NO 2001-6116		20011214
PRIORITY APPLN. INFO.:			US 1999-139321P	P	19990615
			WO 2000-US16498	W	20000615

OTHER SOURCE(S): MARPAT 134:56655

GI



I



II

AB Novel γ-carboline compds. of formula I [R1, R2 = H, acyl, alkyl, cycloalkyl, etc.; R3, R4 = H, OH, amino, CF3, alkyl, etc.; R5-R7 = H, halo, CF3, OH, CN, alkyl, aryl, heterocycle, etc.; X = (substituted) NH, (substituted) CONH, (substituted) NHCO, S; A, B, C = (CH2)n, n = 0-3] are prepared The invention is also concerned with pharmaceutical formulations comprising these novel compds. as active ingredients and the use of the novel compds. and their formulations in the treatment of certain disorders. The compds. of this invention are serotonin agonists and antagonists and are useful in the control or prevention of central nervous system disorders including obesity, anxiety, depression, psychosis, schizophrenia, sleep disorders, sexual disorders, migraine, conditions associated with cephalic pain, social phobias, and gastrointestinal disorders such as dysfunction of the gastrointestinal tract motility (no data). Thus, II is prepared starting from p-fluorothiophenol, β-propiolactone and 1-carbethoxy-4-piperidone. Pharmaceutical compns. containing I are described.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 22 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:419412 HCAPLUS

DOCUMENT NUMBER: 133:110349

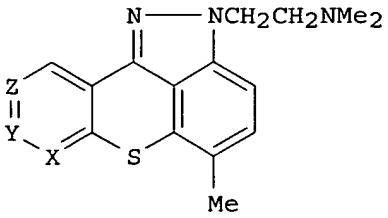
TITLE: Regularities in the temperature-programmed desorption spectra of CO2 and CO from activated carbons

AUTHOR(S): **Haydar, S.**; Moreno-Castilla, C.; Ferro-Garcia, M. A.; Carrasco-Marin, F.; Rivera-Utrilla, J.; Perrard, A.; Joly, J. P.

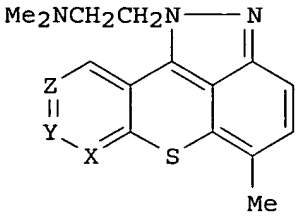
CORPORATE SOURCE: Laboratoire d'Application de la Chimie a l'Environment, UMR 5634 CNRS-Universite Claude Bernard

Lyon 1, Villeurbanne, 69622, Fr.
SOURCE: Carbon (2000), 38(9), 1297-1308
CODEN: CRBNAH; ISSN: 0008-6223
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Temperature-programmed desorption (TPD) spectra of CO and CO2 have been obtained under vacuum or helium flow with activated carbons from different origins and oxidized in various ways. In particular, a special form of TPD, called Intermittent TPD, has been applied to one of the carbon samples (prepared from almond shells and oxidized with nitric acid) in order determine the variation of the apparent activation energy of desorption Ed as the coverage of the surface decreases. Regularities appeared in the set of results obtained: There are common features in TPD profiles of carbons from different origins and histories. This finding is confirmed by a re-examination of numerous CO and CO2 spectra found in the literature, including results obtained under ultra-vacuum. These regularities are interpreted by the existence of the same superficial entities (various oxygen groups with different environments).
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 23 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:146897 HCAPLUS
DOCUMENT NUMBER: 132:279149
TITLE: Synthesis and antitumor activities of 5-methyl-1- and 5-methyl-2-[2-(dimethylamino)ethyl]azabenzothiopyranoindazoles
AUTHOR(S): Krapcho, A. Paul; **Haydar, Simon N.**; Truong-Chiott, Starlan; Hacker, Miles P.; Menta, E.; Beggiolin, G.
CORPORATE SOURCE: Department of Chemistry, University of Vermont, Burlington, VT, 05405, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(3), 305-308
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



II

AB Title compds. I (X = N, Y = Z = CH; Y = N, X = Z = CH; Z = N, X = Y = CH) and II (same X, Y, Z) were prepared Comparisons of the in vitro antitumor activities of the 2-substituted analogs with the benzothiopyranoindazole chemotypes indicate that positioning the nitrogen atom at C-9 (9-aza analog, Z = N) leads to a substrate with potent antitumor activity. The 1-substituted azabenzothiopyranoindazoles, in comparison with the

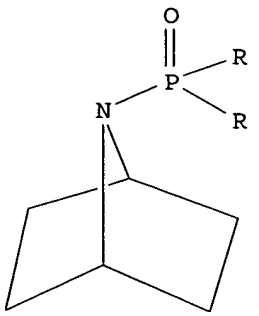
corresponding 2-substituted analogs, exhibit a much lower potency.
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 24 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:712672 HCAPLUS
DOCUMENT NUMBER: 132:64437
TITLE: Total Synthesis of (±)-Epibatidine Using a Biocatalytic Approach
AUTHOR(S): Olivo, Horacio F.; **Hemenway, Michael S.**
CORPORATE SOURCE: Division of Medicinal and Natural Products Chemistry College of Pharmacy and The Center for Biocatalysis and Bioprocessing, The University of Iowa, Iowa City, IA, 52242, USA
SOURCE: Journal of Organic Chemistry (1999), 64(24), 8968-8969 CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:64437
AB (±)-Epibatidine was prepared in 9 steps from trans-4-aminocyclohexanol, via intramol. nucleophilic displacement of a trans-4-aminocyclohexanol derivative, microbial oxidation of an unfunctionalized carbon, and coupling of the chloropyridyl ring to a 7-azanorbornanone.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 25 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:542961 HCAPLUS
TITLE: Microbial hydroxylation of -substituted 7-azabicyclo[2.2.1]heptanes and its application to a total synthesis of epibatidine.
AUTHOR(S): **Hemenway, Michael S.**; Olivo, Horacio F.
CORPORATE SOURCE: Division of Medicinal and Natural Products Chemistry, University of Iowa, Iowa City, IA, 52242, USA
SOURCE: Book of Abstracts, 218th ACS National Meeting, New Orleans, Aug. 22-26 (1999), ORGN-575. American Chemical Society: Washington, D. C. CODEN: 67ZJA5
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB A total synthesis of the natural product and potent non-opioid analgesic epibatidine has been pursued, starting from com. available trans-1,4-aminocyclohexanol hydrochloride, and utilizing microbial hydroxylation via Beauveria bassiana as the key step. A variety of N-substituents have been explored in the hydroxylation step. The hydroxylated metabolite(s) has proved to be a valuable intermediate in this biocatalytic approach to epibatidine. Details concerning the progress toward obtaining epibatidine will be discussed.

L56 ANSWER 26 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:469257 HCAPLUS
DOCUMENT NUMBER: 131:228758
TITLE: Syntheses of New Phosphorus-Containing Azabicycloalkanes and Their Microbial Hydroxylation Using Beauveria bassiana
AUTHOR(S): **Hemenway, Michael S.**; Olivo, Horacio F.
CORPORATE SOURCE: Division of Medicinal Natural Products Chemistry College of Pharmacy and The Center for Biocatalysis and Bioprocessing, The University of Iowa, Iowa City,

IA, 52242, USA
SOURCE: Journal of Organic Chemistry (1999), 64(17), 6312-6318
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:228758
GI

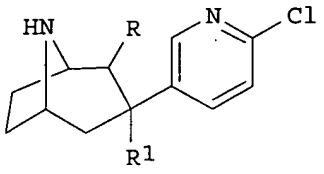


I

AB Representative novel phosphorus-containing azabicyclic substrates I (R = OEt, OPh, Ph) have been synthesized and subsequently microbially hydroxylated in fair to good yields using the microorganism Beauveria bassiana. (7-Azabicyclo[2.2.1]hept-7-yl)phosphonic acid di-Et ester was hydroxylated at the unactivated methylene carbon to give (2-endo-hydroxy-7-azabicyclo[2.2.1]hept-7-yl)phosphonic acid di-Et ester in 43% yield and 64% ee, while N-(diphenylphosphinoyl)-7-azabicyclo[2.2.1]heptane was similarly hydroxylated to give 2-endo-hydroxy-7-(diphenylphosphinoyl)-7-azabicyclo[2.2.1]heptane in 35% yield and 20% ee. (7-Azabicyclo[2.2.1]hept-7-yl)phosphonic acid di-Ph ester yielded two distinct hydroxylated products:monohydroxylated (2-endo-hydroxy-7-azabicyclo[2.2.1]-hept-7-yl)phosphonic acid di-Ph ester in 7% yield and 7% ee and dihydroxylated (2-endo-hydroxy-7-azabicyclo[2.2.1]hept-7-yl)phosphonic acid Ph, p-hydroxyphenyl ester in 37% yield and 77% ee. HPLC studies indicated that the monohydroxylated metabolite is formed first during fermentation, and becomes a substrate for a second enzymic hydroxylation at one of the aromatic rings with induced enantioselection, to give the dihydroxylated metabolite. All microbially hydroxylated metabolites were easily N-deprotected using TFA-CH2Cl2 (1:1). Thus, N-phosphinyl groups are good facilitators of hydroxylation reactions with B. bassiana and offer a new choice for an N-substituent when substrates are hydroxylated with this microorganism. By offering a new N-substituent, this work extends the general utility of B. bassiana as a preparatively useful unactivated methylene hydroxylator.
REFERENCE COUNT: 105 THERE ARE 105 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 27 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:298770 HCAPLUS
DOCUMENT NUMBER: 131:130150
TITLE: Syntheses of New Open-Ring and homo-Epibatidine Analogs from Tropinone

AUTHOR(S): Olivo, Horacio F.; Colby, David A.; **Hemenway, Michael S.**
CORPORATE SOURCE: Division of Medicinal and Natural Products Chemistry College of Pharmacy, The University of Iowa, Iowa City, IA, 52242, USA
SOURCE: Journal of Organic Chemistry (1999), 64(13), 4966-4968 CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:130150
GI



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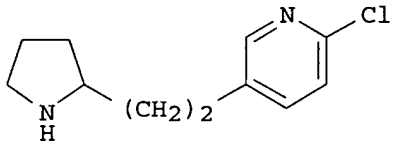
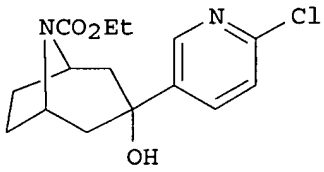


II



III

AB The synthesis of sym. homo I (R = R1 = H), dehydro homo I (RR1 = bond) and open ring analog II of epibatidine was accomplished from tropinone. The intermediate III was converted to an open ring analog via a novel ionic hydrogenation.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 28 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:90334 HCAPLUS
DOCUMENT NUMBER: 130:153977
TITLE: Preparation of (azacycloalkyl)alkanoyl peptides as inhibitors of platelet aggregation and thrombosis
INVENTOR(S): Klein, Scott I.; **Molino, Bruce F.**
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA
SOURCE: U.S., 21 pp., Cont.-in-part of U.S. Ser. No. 138,820, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5866685	A	19990202	US 1996-628648	19960502
WO 9510295	A1	19950420	WO 1994-US12135	19941017

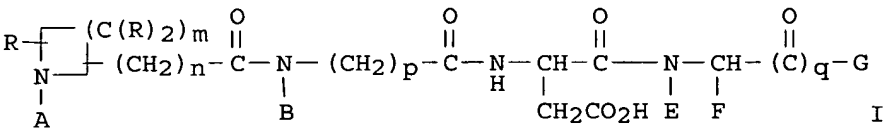
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU,

MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 5780590	A	19980714	US 1996-700950	19960821
US 6274705	B1	20010814	US 1998-137998	19980821
US 2002002268	A1	20020103	US 2001-903813	20010712
US 6797700	B2	20040928		
PRIORITY APPLN. INFO.:			US 1993-138820	B2 19931015
			WO 1994-US12135	W 19941017
			US 1993-13820	B2 19931015
			US 1995-476750	A2 19950607
			US 1996-628648	A1 19960502
			US 1998-137998	A3 19980821

OTHER SOURCE(S): MARPAT 130:153977

GI



AB Title compds. [I; R = H, alkyl, aryl, aralkyl; A = H, (substituted) amidino; B = alkyl, cycloalkyl, cycloalkylalkyl, alkylcycloalkyl, alkylcycloalkylalkyl, aryl, aralkyl, alkylaryl, alkylaralkyl; E = H; EF = atoms to form 4-7 membered azacycloalkane ring; F = H, side chain of a naturally occurring α-amino acid, alkyl, cycloalkyl, cycloalkylalkyl, alkylcycloalkyl, alkylcycloalkylalkyl, (substituted) aryl, (substituted) aralkyl, (substituted) heterocyclyl, (substituted) heterocyclylalkyl; G = alkyl, cycloalkyl, cycloalkylalkyl, alkylcycloalkyl, alkylcycloalkylalkyl, (substituted) aryl, (substituted) aralkyl, (substituted) heterocyclyl, (substituted) heterocyclylalkyl, OR1, NR1R2; R1, R2 = H, alkyl, cycloalkyl, cycloalkylalkyl, alkylcycloalkyl, alkylcycloalkylalkyl, aryl, aralkyl, alkylaryl, alkylaralkyl; q = 0, 1; m = 1-5; n = 0-6; p = 1-4] were prepared For example, N-[N-[N-(4-(piperidin-4-yl)butanoyl)-N-ethylglycyl]aspartyl]-β-cyclohexylalanine was prepared from BocN(Et)CH2CO2H, Boc-Asp(OCH2Ph)-OH, β-cyclohexylalanine and Me 4-(N-Boc-piperidine-4-yl)crotonate using solution phase procedures. Platelet aggregation and fibrinogen-binding assays were performed on I (incomplete data).

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 29 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:762441 HCAPLUS

DOCUMENT NUMBER: 130:57581

TITLE: Study of the evolution of carbon dioxide from active carbon by a threshold temperature-programmed desorption method

AUTHOR(S): **Haydar, S.**; Joly, J. P.

CORPORATE SOURCE: Laboratoire d'Application de la Chimie a I'Environnement (UMR 5634), CNRS-Universite Claude Bernard Lyon 1, Villeurbanne, 69622, Fr.

SOURCE: Journal of Thermal Analysis and Calorimetry (1998), 52(2), 345-353
CODEN: JTACF7; ISSN: 1418-2874

PUBLISHER: Kluwer Academic Publishers

DOCUMENT TYPE: Journal
LANGUAGE: English
AB A particular Temperature-Programmed Desorption (TPD) method, called 'Intermittent TPD', has been applied to the decomposition of oxygen groups naturally present at the surface of a microporous active carbon. It is shown that this method provides more information on the kinetics of the thermal decomposition of these species than the classical TPD technique. The main result is that the decomposition of these oxygen groups occurs in at least 7 distinct stages which have been characterized by their apparent activation energy and the corresponding frequency factor. The present study underlines the usefulness of ITPD for studying the rate of desorption of gases from powdered samples with a strongly heterogeneous surface.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 30 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:699917 HCAPLUS
DOCUMENT NUMBER: 130:24947
TITLE: Unexpected displacements of chloride by bromide found during Sandmeyer reactions of 3- or 5-amino-2-chloropyridines
AUTHOR(S): Krapcho, A. Paul; **Haydar, Simon N.**
CORPORATE SOURCE: Department of Chemistry, The University of Vermont, Burlington, VT, 05405, USA
SOURCE: Heterocyclic Communications (1998), 4(4), 291-292
CODEN: HCOMEX; ISSN: 0793-0283
PUBLISHER: Freund Publishing House Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Facile, temperature dependent displacements of chloride by bromide have been found in the diazotizations of 3-amino-2-chloropyridine or 5-amino-2-chloropyridine, followed by addition of CuBr in 48% HBr, which lead to good yields of the unexpected 2,3-dibromopyridine or 2,5-dibromopyridine, resp.
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 31 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:479050 HCAPLUS
DOCUMENT NUMBER: 129:122869
TITLE: Antithrombotic azacycloalkylalkanoyl peptides and pseudopeptides
INVENTOR(S): Klein, Scott I.; **Molino, Bruce F.**; Czekaj, Mark; Gardner, Charles J.
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA
SOURCE: U.S., 29 pp., Cont.-in-part of U.S. Ser. No. 476,750.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5780590	A	19980714	US 1996-700950	19960821
US 5866685	A	19990202	US 1996-628648	19960502
CA 2263732	AA	19980430	CA 1997-2263732	19970815
WO 9817678	A1	19980430	WO 1997-US14578	19970815

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,

DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US,
UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
GN, ML, MR, NE, SN, TD, TG

AU 9740749	A1	19980515	AU 1997-40749		19970815
AU 722112	B2	20000720			
EP 929572	A1	19990721	EP 1997-938424		19970815
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO					
BR 9711205	A	19990817	BR 1997-11205		19970815
CN 1231671	A	19991013	CN 1997-198164		19970815
NZ 334059	A	20000128	NZ 1997-334059		19970815
AP 904	A	20001124	AP 1999-1452		19970815
W: GH, KE, LS, MW, SD, SZ, UG, ZW					
JP 2001501965	T2	20010213	JP 1998-519340		19970815
ZA 9707511	A	19980303	ZA 1997-7511		19970821
KR 2000035797	A	20000626	KR 1999-701363		19990219
NO 9900836	A	19990420	NO 1999-836		19990222
PRIORITY APPLN. INFO.:			US 1993-138820	B2	19931015
			US 1995-476750	A2	19950607
			US 1996-628648	A1	19960502
			WO 1994-US12135	W	19941017
			US 1996-700950	A	19960821
			WO 1997-US14578	W	19970815

OTHER SOURCE(S): MARPAT 129:122869

AB Peptides P2NB(CH2)pCONHCH(CH2CO2P1)CONE1CHE2COG [B = alkyl, cycloalkyl, cycloalkylalkyl, alkylcycloalkyl, alkylcycloalkylalkyl, aryl, aralkyl, alkylaryl, alkylalkyl; E1 = H or E1NCHE2 is azacycloalkyl; E2 = α-carbon side chain of a naturally occurring α-amino acid, H, alkyl, cycloalkyl, aryl, etc.; G = OR1 or NR1R2 (R1, R2 = H, alkyl, cycloalkyl, aryl, etc.); p = 1-4; P1 is a hydrogenation labile acid protecting group; P2 is an acid labile amine protecting group or TFA,H] were prepared as antithrombotics. N-[N-[N-(4-piperdin-4-ylbutanoyl)-N-ethylglycyl]-L-aspartyl]-L-β -cyclohexylalaninamide was prepared and had IC50 = 0.097 μM for inhibition of platelet aggregation.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 32 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:429224 HCAPLUS
DOCUMENT NUMBER: 129:49374
TITLE: Design of a New Class of Orally Active Fibrinogen Receptor Antagonists
AUTHOR(S): Klein, Scott I.; **Molino, Bruce F.**; Czekaj, Mark; Gardner, Charles J.; Chu, Valeria; Brown, Karen; Sabatino, Ralph D.; Bostwick, Jeffrey S.; Kasiewski, Charles; Bentley, Ross; Windisch, Vincent; Perrone, Mark; Dunwiddie, Christopher T.; Leadley, Robert J.
CORPORATE SOURCE: Department of Cardiovascular Research, Rhone-Poulenc Rorer Central Research, Collegeville, PA, 19426, USA
SOURCE: Journal of Medicinal Chemistry (1998), 41(14), 2492-2502
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The integrin receptor recognition sequence Arg-Gly-Asp was successfully

used as a template from which to develop a series of potent, selective, orally active, peptide-based fibrinogen receptor antagonists with a long duration of action. Simple modifications centered on the Arg and Gly residues quickly led to a modified peptide, R(CH2)nCONEtCH2CO-L-Asp-L-Val-OH [I, R = NHC(:NH)NH2, n = 5, II] with significantly enhanced ability to inhibit in vitro platelet aggregation. Substitution of the guanidino group in II provided I [R = 4-piperidinyl, n = 3] which showed not only further increase in potency but also a modest degree of oral efficacy. Finally, exploration of the nature of the C-terminal amino acid, with respect to its side-chain functionality and the carboxy terminus, yielded a group of mols. that showed excellent in vitro potency for inhibiting platelet aggregation, excellent integrin selectivity, a high level of oral efficacy, and an extended duration of action.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 33 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:268512 HCAPLUS
DOCUMENT NUMBER: 129:4865
TITLE: Preparation of antithrombotic azacycloalkylalkanoyl peptides and pseudopeptides
INVENTOR(S): Klein, Scott I.; **Molino, Bruce F.**; Czekaj, Mark; Gardner, Charles J.
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA; Klein, Scott I.; Molino, Bruce F.; Czekaj, Mark; Gardner, Charles J.
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9817678	A1	19980430	WO 1997-US14578	19970815
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5780590	A	19980714	US 1996-700950	19960821
CA 2263732	AA	19980430	CA 1997-2263732	19970815
AU 9740749	A1	19980515	AU 1997-40749	19970815
AU 722112	B2	20000720		
EP 929572	A1	19990721	EP 1997-938424	19970815
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
BR 9711205	A	19990817	BR 1997-11205	19970815
NZ 334059	A	20000128	NZ 1997-334059	19970815
AP 904	A	20001124	AP 1999-1452	19970815
W: GH, KE, LS, MW, SD, SZ, UG, ZW				
JP 2001501965	T2	20010213	JP 1998-519340	19970815
NO 9900836	A	19990420	NO 1999-836	19990222
PRIORITY APPLN. INFO.:			US 1996-700950 A	19960821
			US 1993-138820 B2	19931015
			US 1995-476750 A2	19950607

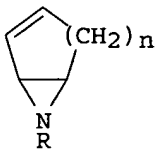
US 1996-628648 A1 19960502
WO 1997-US14578 W 19970815

OTHER SOURCE(S): MARPAT 129:4865

AB The invention is directed to a non-hygroscopic stable crystalline form of the antithrombotic compound N-[N-[N-[4-(piperidin-4-yl)butanoyl]-N-ethylglycyl]-L-aspartyl]-L-β-cyclohexyl-alanine amide (I), to processes for preparing said stable crystalline form, to a pharmaceutical composition thereof, and intermediates thereof. The invention is directed also to processes and intermediates for preparing a compound of formula P2'N(B)(CH2)pCONHCH(CH2CO2P1)CON(E1)CH(E2)COG [B = alkyl, cycloalkyl, cycloalkylalkyl, alkylcycloalkyl, alkylcycloalkylalkyl, aryl, aralkyl, alkylaryl, alkylaralkyl; E1 = H; E2 = the α-carbon side chain of a naturally occurring α-amino acid, H, alkyl, cycloalkyl, cycloalkylalkyl, alkylcycloalkyl, (un)substituted aryl, (un)substituted aralkyl, (un)substituted heterocyclyl, (un)substituted heterocyclylalkyl; or E1 and E2 taken together with the nitrogen and carbon atoms through which E1 and E2 are linked form a 4, 5-, 6-, or 7-membered ring; G = OR1, NR1R2; wherein R1, R2 = H, alkyl, cycloalkyl, cycloalkylalkyl, alkylcycloalkyl, alkylcycloalkyl, aryl, aralkyl, alkylaryl, alkylaralkyl; p = 1-4; P1 = a hydrogenation-labile acid protecting group; P2' = P2, CF3CO2H.H; P2 = an acid-labile amine protecting group]. Thus, 4-(1-benzyloxycarbonyl-4-piperidinylene)butyric acid (preparation given) was condensed with Et-Gly-Asp(OBzl)-Cha-NH2.CF3CO2H (Cha = β-cyclohexyl-L-alanine) using (2-1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate and (Me2CH)2NEt in DMF to give RNEtCH2CO-Asp(OBzl)-Cha-NH2 [R = 4-(1-benzyloxycarbonyl-4-piperidinylene)butyroyl] in 83% yield, which was hydrogenated by ammonium formate in the presence of 10% Pd-C in a mixture of EtOH, iPrOH, and H2O at 40-50° for 5 h to give hygroscopic crystalline form of I in 84.8% yield. Hygroscopic crystalline form of I (7.45 kg) was milled in a hammer mill. The resulting solid (7.35 kg) was placed in a stainless steel drier tray and the tray was covered with perforated aluminum foil, then sealed into a humidity oven, kept sealed throughout the form conversion at 40%RH and 60° for 1 h, 80% RH and 60° for 12 h, and then at 40% RH and 60° for 2 h to give non-hygroscopic crystalline form of I in 96.6% yield. I showed IC50 of 0.097 μM for inhibiting human fibrinogen-induced aggregation of human platelet vs. 0.047 μM for N-[4-(4-piperidyl)butanoyl]-glycyl-L-aspartyl-L-tryptophan.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 34 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:178676 HCAPLUS
DOCUMENT NUMBER: 128:282744
TITLE: New preparation of activated 2-vinylaziridines from δ-amino alcohols
AUTHOR(S): Olivo, Horacio F.; **Hemenway, Michael S.**; Hartwig, Amy C.; Chan, Raymond
CORPORATE SOURCE: Division Medicinal Natural Products Chemistry, College Pharmacy, University Iowa, Iowa City, IA, 52242, USA
SOURCE: Synlett (1998), (3), 247-248
CODEN: SYNLES; ISSN: 0936-5214
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 128:282744
GI



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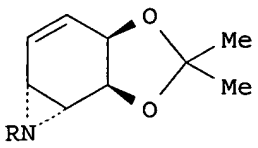
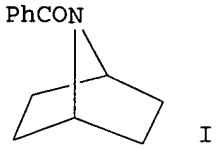


II

AB Activated vinylaziridines I (R = PhCO, n = 1-3; R = PhCH2O2C, n= 2; R = 4-tosyl, n = 2) and II (R = PhCO, PhCH2O2C, Me3CO2C) were prepared from appropriate cis-1-aminocycloalk-2-en-4-ols by using Mitsunobu conditions.

L56 ANSWER 35 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:160361 HCAPLUS
DOCUMENT NUMBER: 128:230549
TITLE: Synthesis and microbial hydroxylation of some azabicycloalkanes
AUTHOR(S): Olivo, Horacio F.; **Hemenway, Michael S.**; Gezginci, Mikail H.
CORPORATE SOURCE: Division of Medicinal and Natural Products Chemistry, College of Pharmacy, The University of Iowa, Iowa City, IA, 52242, USA
SOURCE: Tetrahedron Letters (1998), 39(11), 1309-1312
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 128:230549
GI



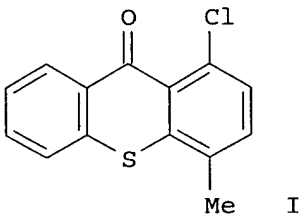
I

AB N-Substituted 7-azabicyclo[2.2.1]heptanes, e.g. I, were synthesized in a short route. These compds. containing benzamide or benzenesulfonamide groups are good substrates for microbial oxidation of unactivated carbons by B. bassiana.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 36 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:752575 HCAPLUS
DOCUMENT NUMBER: 128:84036
TITLE: Conformationally flexible platelet aggregation inhibitors based on the tetrapeptide Arg-Gly-Asp-Arg
AUTHOR(S): Klein, S. I.; Czekaj, M.; **Molino, B. F.**; Chu, V.
CORPORATE SOURCE: Department of Cardiovascular Research, Rhone-Poulenc Rorer, Collegeville, PA, 19426, USA
SOURCE: European Journal of Medicinal Chemistry (1997), 32(10), 833-839
CODEN: EJMCA5; ISSN: 0223-5234

PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of nonpeptide fibrinogen receptor antagonists based upon the tetrapeptide Arg-Gly-Asp-Arg were prepared These relatively simple derivs. incorporate a high degree of conformational flexibility that was anticipated to allow them to attain the requisite conformation for binding to the platelet fibrinogen receptor. Optimization of the distances between the required acidic and basic functional groups led eventually to compound which is a 100-fold more potent inhibitor of platelet aggregation than the peptide it is based upon.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 37 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:751985 HCAPLUS
DOCUMENT NUMBER: 128:48170
TITLE: N,N,5-Trimethyl-1H-[1]benzothiopyrano[4,3,2-cd]indazole-1-ethanamine - a novel heterocycle
AUTHOR(S): Krapcho, A. Paul; **Haydar, Simon N.**
CORPORATE SOURCE: Department of Chemistry, University of Vermont, Burlington, VT, 05405, USA
SOURCE: Journal of Heterocyclic Chemistry (1997), 34(5), 1637-1638
CODEN: JHTCAD; ISSN: 0022-152X
PUBLISHER: HeteroCorporation
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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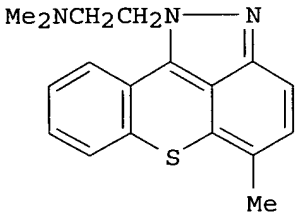

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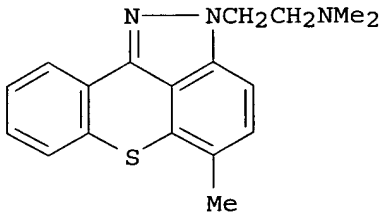
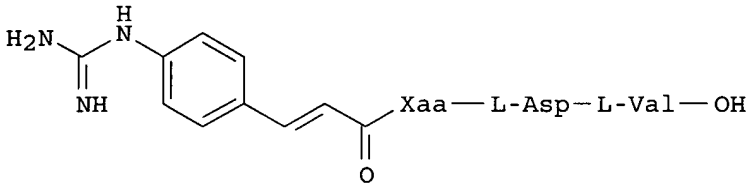


III

AB Treatment of thioxanthenone I with [2-(dimethylamino)ethyl]hydrazine led to benzothiopyranoindazole II, a novel heterocycle, along with its expected isomer (III).
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 38 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:469001 HCAPLUS
DOCUMENT NUMBER: 127:162104

TITLE: Constrained β-alanine based GpIIb/IIIa antagonists
AUTHOR(S): Klein, Scott I.; Czekaj, Mark; **Molino, Bruce F.**; Chu, Valeria
CORPORATE SOURCE: Rhone-Poulenc Rorer, Departments of Cardiovascular Chemistry and Biology, Collegeville, PA, 19426, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(13), 1773-1778
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

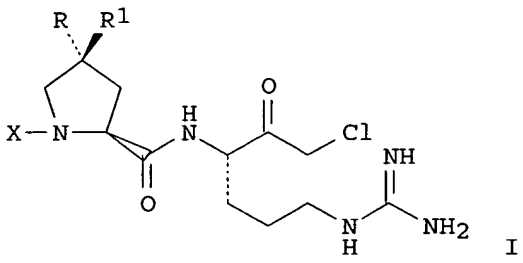


I

AB A series of novel fibrinogen receptor antagonists, e.g. I (Xaa = N-Et β-alanine, (R)-2-pyrrolidineacetic acid, (R)-2-piperidineacetic acid, (S)-3-pyrrolidinecarboxylic acid, (S)-2-azetidineacetic acid) has been synthesized following the design principles of centrally constrained and peptide based fibrinogen receptor antagonists. The centrally constrained β-alanine based RGD mimics I have been demonstrated to be potent inhibitors of platelet aggregation.
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 39 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1997:162128 HCAPLUS
TITLE: Regioisomeric azabenzothiopyranoindazoles. Synthesis and antitumor evaluations.
AUTHOR(S): Krapcho, A. Paul; **Haydar, Simon N.**; Hacker, Miles P.; Truong-Chiott, Starlan; Menta, Ernesto
CORPORATE SOURCE: Department Chemistry, University Vermont, Burlington, VT, 05405, USA
SOURCE: Book of Abstracts, 213th ACS National Meeting, San Francisco, April 13-17 (1997), MEDI-296. American Chemical Society: Washington, D. C.
CODEN: 64AOAA
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB A number of benzothiopyranoindazoles have been synthesized in order to avoid enzymically mediated radical cycling and specific chemotypes exhibited broad-spectrum antitumor activities. At part of a program to develop new chemotypes, we have replaced the carbon atom of the benzothiopyranoindazole skeleton at positions 7, 8 and 9 with a nitrogen atom leading to the 7-aza-, 8-aza- and 9-azabenzothiopyranoindazoles. The synthesis of the 10-aza regioisomer is currently under investigation. The antitumor activities, which are highly dependent on the position of the nitrogen atom and the side arm structure (R and R1), will be discussed. Several promising candidates for preclin. trials have been identified.

L56 ANSWER 40 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:604560 HCAPLUS
DOCUMENT NUMBER: 125:301564
TITLE: O-benzyl hydroxyproline as a bioisostere for Phe-Pro: Novel dipeptide thrombin inhibitors
AUTHOR(S): Klein, Scott I.; Dener, Jeffrey M.; **Molino, Bruce F.**; Gardner, Charles J.; D'Alisa, Rose; Dunwiddie, Christopher T.; Kasiewski, Charles; Leadley, Robert J.
CORPORATE SOURCE: Department Medicinal Chemistry, Rhone-Poulenc Rorer, Collegeville, PA, 19426, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1996), 6(18), 2225-2230
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB A series of thrombin inhibitors I [X = H-D-Phe, Ph(CH2)2CO, Ac, Et, MeSO2; R = H, PhCH2O, cyclohexylmethoxy, BuO, Ph(CH2)3O, Ph2CH(CH2)2O; R1 = H, OCH2Ph], based on the known inhibitor PPACK (I; X = H-D-Phe, R = R1 = H) in which the D-Phe-Pro dipeptide has been replaced, were prepared and tested. I (X = Ac, R = PhCH2O, R1 = H) is a more potent inhibitor of thrombin, and is more selective, than PPACK itself.

L56 ANSWER 41 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:398914 HCAPLUS
DOCUMENT NUMBER: 125:131632
TITLE: Non-peptide fibrinogen receptor antagonists based upon a 4-substituted piperidine scaffold
AUTHOR(S): Klein, Scott; **Molino, Bruce F.**; Czekaj, Mark; Dener, Jeffrey S.; Leadley, Robert J.; Sabatino, Ralph; Dunwiddie, Christopher T.; Chu, Valeria
CORPORATE SOURCE: Rhone-Poulenc Rorer, Dep. Medicinal Chem., Collegeville, PA, 19426, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1996), 6(12), 1403-1408
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 125:131632
AB Structure-activity relationships developed from work with peptide based fibrinogen receptor antagonists have been successfully applied to the development of simple and highly potent nonpeptide agents of the same class.

L56 ANSWER 42 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:389613 HCAPLUS
DOCUMENT NUMBER: 125:66726
TITLE: An integrated approach to observe the evolution of pollutants in reservoirs
AUTHOR(S): Copertino, V.A.; de Bernardinis, B.; **Molino, B.**; Telesca, V.; Singh, V.P.
CORPORATE SOURCE: Department of Engineering and Environmental Physics, University of Basilicata, Potenza, 85100, Italy
SOURCE: Water Science and Technology Library (1996), 16(Vol. 3, Water-Quality Hydrology), 43-55
CODEN: WSTLEQ; ISSN: 0921-092X
PUBLISHER: Kluwer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A method for combining monitoring, math. modeling, and the use of a geog. information system (GIS) is proposed to investigate the transport, dispersion and diffusion of pollutants in reservoirs. Preliminary and partial results obtained from an extensive and continuous observation and measurement activity on the Camastra reservoir have confirmed the validity of the proposed approach.

L56 ANSWER 43 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:968156 HCAPLUS
DOCUMENT NUMBER: 124:41821
TITLE: Bis(5-chloro-2-nitrophenyl) disulfide
AUTHOR(S): Garcia, J. Gabriel; **Haydar, Simon N.**; Krapcho, A. Paul; Fronczek, Frank R.
CORPORATE SOURCE: Dep. Chem., Univ. Vermont, Berlington, VT, 05405-0125, USA
SOURCE: Acta Crystallographica, Section C: Crystal Structure Communications (1995), C51(11), 2333-5
CODEN: ACSCEE; ISSN: 0108-2701
PUBLISHER: Munksgaard
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The title mol., C12H6Cl2N2O4S2, lies on a 2-fold axis in the crystal. The C-S-S-C group has a skewed nonplanar conformation with a torsion-angle magnitude of 86.7(1)°. The S-S-C bond angle is 104.11(5)°, and the S-S, S-C, C-N, and C-Cl bond lengths are 2.0432(5), 1.789(1), 1.462(2) and 1.726(1) Å, resp. The nitro group is rotated 15.2(2)° out of the plane of the Ph ring. Crystallog. data and atomic coordinates are given.

L56 ANSWER 44 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:886373 HCAPLUS
DOCUMENT NUMBER: 123:306599
TITLE: Antithrombotic azacycloalkylalkanoyl peptides and pseudopeptides
INVENTOR(S): Klein, Scott I.; **Molino, Bruce F.**
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9510295	A1	19950420	WO 1994-US12135	19941017
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2174097	AA	19950420	CA 1994-2174097	19941017
CA 2174097	C	20020604		
HU 73856	A2	19960930	HU 1996-983	19941017
CN 1135717	A	19961113	CN 1994-194242	19941017
BR 9407839	A	19970513	BR 1994-7839	19941017
EP 812205	A1	19971217	EP 1995-900403	19941017
EP 812205	B1	20010314		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
AU 703854	B2	19990401	AU 1994-81237	19941017
AU 9481237	A1	19950504		
RU 2134695	C1	19990820	RU 1996-109375	19941017
RO 115520	B1	20000330	RO 1996-812	19941017
JP 3032297	B2	20000410	JP 1995-512250	19941017
JP 09507213	T2	19970722		
AT 199727	E	20010315	AT 1995-900403	19941017
ES 2155122	T3	20010501	ES 1995-900403	19941017
PT 812205	T	20010830	PT 1995-900403	19941017
PL 181749	B1	20010928	PL 1994-313975	19941017
CZ 291378	B6	20030212	CZ 1996-1084	19941017
FI 9601634	A	19960523	FI 1996-1634	19960412
NO 9601460	A	19960617	NO 1996-1460	19960412
BG 63166	B1	20010531	BG 1996-100544	19960426
US 5866685	A	19990202	US 1996-628648	19960502
HK 1006225	A1	20011207	HK 1998-105458	19980616
US 6274705	B1	20010814	US 1998-137998	19980821
GR 3035581	T3	20010629	GR 2001-400194	20010315
US 2002002268	A1	20020103	US 2001-903813	20010712
US 6797700	B2	20040928		
PRIORITY APPLN. INFO.:			US 1993-138820	A 19931015
			US 1993-13820	B2 19931015
			WO 1994-US12135	W 19941017
			US 1996-628648	A1 19960502
			US 1998-137998	A3 19980821

OTHER SOURCE(S): MARPAT 123:306599

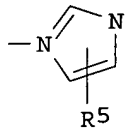
AB The present invention relates to azacycloalkylakanoyl peptides and pseudopeptides which inhibit platelet aggregation and thrombus formation thereby being useful in the prevention and treatment of thrombosis associated with disease states such as myocardial infarction, stroke, peripheral arterial disease, and disseminated intravascular coagulation, to methods for the prevention or treatment of thrombosis in a mammal in need of such therapy comprising the administration of a therapeutically effective amount of such compds., and to pharmaceutical compns. comprising such compds.

L56 ANSWER 45 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:511411 HCAPLUS
DOCUMENT NUMBER: 122:291536
TITLE: Preparation of antithrombotic peptides and pseudopeptides.
INVENTOR(S): Klein, Scott I.; **Molino, Bruce F.**; Czekaj, Mark; Gardner, Charles; Becker, Michael R.; Dener, Jeffrey M.; Pelletier, Jeffrey C.
PATENT ASSIGNEE(S): USA

SOURCE: U.S., 24 pp. Cont.-in-part of U.S. Ser. No. 677,006, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5332726	A	19940726	US 1992-859779	19920330
US 4952562	A	19900828	US 1989-415006	19890929
PRIORITY APPLN. INFO.:			US 1989-415006 A2	19890929
			US 1990-460777 B2	19900104
			US 1990-534385 B2	19900607
			US 1991-677006 B2	19910328

OTHER SOURCE(S): MARPAT 122:291536
GI

Q1= 

AB A(CH2)m1(CR1R2)h1Bk(CR3R4)h2(CH2)m2DCH[(CH2)nCO2H]COZ [A = cyano, Q1, (NH)xC(N:R5)(NH)x1R6, etc.; B, D = CH2NH, CH2S, CH2O, etc.; Z = OR6, N-containing heterocyclyl, amino acid or dipeptide residue, etc.; R1-R6 = H, alkyl, cycloalkyl, cycloalkylmethyl, (substituted) aryl, aralkyl; h1, h2, k = 0,1; m1, m2 = 0-9; n = 1-3; x, x1 = 0,1], were prepared Thus, arginylglycylaspartylisobutylamide (solution phase preparation given) inhibited fibrinogen-mediated platelet aggregation with IC50 = 3.6 μM.

L56 ANSWER 46 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1995:64620 HCAPLUS
DOCUMENT NUMBER: 122:23449
TITLE: Antithrombotic activity of a linear conformationally flexible RGD mimic
AUTHOR(S): Klein, Scott I.; **Molino, Bruce F.**; Czekaj, Mark; Chu, Valeria; Ruggeri, Zaverio; Cook, Jacquelynn J.; Bostwick, Jeffrey S.; Kasiewski, Charles
CORPORATE SOURCE: Rhone-Poulenc Rorer Cent. Res., Collegeville, PA, 19426, USA
SOURCE: Pept. 1992, Proc. Eur. Pept. Symp., 22nd (1993), Meeting Date 1992, 635-6. Editor(s): Schneider, Conrad H.; Eberle, Alex N. ESCOM: Leiden, Neth.
CODEN: 60LUAN
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Elimination of the terminal amino group, lengthening of the arginine side chain by one C atom, and N-alkylation of the Arg-Gly amide bond provided an analog of the parent peptide RGDV, RG 13965. RG 13965 represents a relatively simple and highly effective class of peptide-derived antithrombotic agents which may prove to be clin. useful.

L56 ANSWER 47 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:646328 HCAPLUS
DOCUMENT NUMBER: 121:246328
TITLE: Compounds having cholecystokinin and gastrin antagonistic properties
INVENTOR(S): Ewing, William R.; **Molino, Bruce F.**
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA
SOURCE: U.S., 16 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5340801	A	19940823	US 1991-697177	19910508
PRIORITY APPLN. INFO.:			US 1991-697177	19910508

OTHER SOURCE(S): MARPAT 121:246328
AB This invention relates to preparation of N-arylcarbamoylproline analogs which are useful as cholecystokinin and gastrin antagonists and their use in preventing or treating cholecystokinin- or gastrin-related disorders of the gastrointestinal, central nervous, or appetite regulatory systems. For example, 2-[[N-(3-methyl)phenylcarbamoyl-4R-benzyloxy]-L-prolyl]-1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole was prepared by 3 steps from N-α-tert-butoxycarbonyl-O-benzyl-L-4-hydroxyproline and 1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole and subjected for in vitro CCK-A receptor and gastrin receptor binding assays.

L56 ANSWER 48 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:622204 HCAPLUS
DOCUMENT NUMBER: 121:222204
TITLE: Highly potent and selective gastrin receptor antagonists based on CCK-4
AUTHOR(S): Ewing, W. Richard; **Molino, Bruce F.**; Bolton, Scott A.; Manetta, Vincent; Pendley, Charles; Capilino, Alison
CORPORATE SOURCE: Rhone-Poulenc Rorer Cent. Res., Collegeville, PA, 19426, USA
SOURCE: Pept. 1992, Proc. Eur. Pept. Symp., 22nd (1993), Meeting Date 1992, 619-20. Editor(s): Schneider, Conrad H.; Eberle, Alex N. ESCOM: Leiden, Neth.
CODEN: 60LUAN
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Effects were investigated of substituting the C-terminal Asp on a CCK-4-based gastrin receptor antagonist. Cyclic diacids gave more potent antagonists and displayed better selectivity for the gastrin receptor over the CCK-A receptor.

L56 ANSWER 49 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:670633 HCAPLUS
DOCUMENT NUMBER: 119:270633
TITLE: Preparation of antithrombotic diaminoalkanoic acid derivatives
INVENTOR(S): Klein, Scott I.; **Molino, Bruce F.**
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer International (Holdings) Inc., USA
SOURCE: PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9311759	A1	19930624	WO 1992-US10535	19921207
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
US 5258398	A	19931102	US 1991-808400	19911216
AU 9332421	A1	19930719	AU 1993-32421	19921207
PRIORITY APPLN. INFO.:			US 1991-808400 A	19911216
			WO 1992-US10535 A	19921207

OTHER SOURCE(S): MARPAT 119:270633
AB (ANH)A1NHCH(CH2)pCO2H [A, A1 = alkanoyl, alkenoyl, D- or L-α-amino acid residue, XGMn; X = NR1R2, NR1C(:NR2)NHR3, C(:NR1)NHR2, R1-substituted imidazol-1-yl; G = alkanoyl, alkenoyl, (substituted) PhCO, phenylalkanoyl, phenylalkenoyl, etc.; M = NR4CH2CO; n = 0, 1; p = 1-3; R1-R4 = H, alkyl; with provisos], were prepared Thus, 8-guanidinooctanoic acid was nitrated with fuming HNO3/fuming H2SO4 and the product was condensed with aspartic acid amide β-benzyl ester using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride and 1-hydroxybenzotriazole to give N-α-8-(nitroguanidino)octanoylaspartic acid amide β-benzyl ester. This was stirred with iodobenzene bistrifluoroacetate in MeCN/H2O to give benzyl N-8-nitroguanidinooctanoyl-3,3-diaminopropionate, which was condensed with 8-nitroguanidinooctanoic acid followed by hydrogenolysis to give N,N'-bis(8-guanidinooctanoyl)-3,3-diaminopropionic acid. This inhibited fibrinogen-mediated platelet aggregation and 125I-fibrinogen binding to platelets with IC50's of 0.12 and 0.07 μM, resp.

L56 ANSWER 50 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:531274 HCAPLUS
DOCUMENT NUMBER: 119:131274
TITLE: The gastrin/cholecystokinin-B receptor antagonist L-365,260 reduces basal acid secretion and prevents gastrointestinal damage induced by aspirin, ethanol and cysteamine in the rat
AUTHOR(S): Pendley, Charles E.; Fitzpatrick, Leo R.; Ewing, Richard W.; **Molino, Bruce F.**; Martin, Gregory E.
CORPORATE SOURCE: Dep. Pharmacol., Rhone-Poulenc Rorer Cent. Res., Collegeville, PA, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1993), 265(3), 1348-54
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: English
AB L-365,260, a nonpeptide antagonist of gastrin/CCK-B receptors, was evaluated in receptor binding, antisecretory and gastrointestinal damage assays. L-365,260 binds potently and stereo-selectively to gastrin and CCK-B sites in guinea pig tissue. In contrast, L-365,260 binds to the isolated canine parietal cell gastrin receptor weakly, and without stereoselectivity. In the pylorus-ligated rat, low doses of L-365,260, given i.v., attenuated pentagastrin-stimulated acid secretion, whereas higher doses were required to inhibit both histamine-stimulated and basal acid secretion. In an aspirin-induced gastric damage model, L-365,260 was 2.4-fold less potent than the standard histamine H2 antagonist cimetidine in preventing gastric damage when given i.v., and was 8.3-fold less potent

than cimetidine when give p.o. Moreover, the ED50 value for L-365,260, given i.v., in prevention of aspirin-induced gastric damage (11.5 mg/kg) agreed well with its ED50 value for inhibition of basal acid secretion (12.6 mg/kg). At doses as great as 100 mg/kg p.o., neither L-365,260 nor cimetidine had an effect on ethanol-induced gastric damage. L-365,260, although oral less bioavailable relative to cimetidine in the aspirin gastric damage model, was as potent as cimetidine in the prevention of cysteamine-induced duodenal ulcers in the rat. Thus, the gastrin/CCK-B receptor antagonist L-365,260, at doses supramaximal for the inhibition of pentagastrin-stimulated secretory responses in vivo, inhibits gastrointestinal damage of models of peptic ulcer disease by an antisecretory mechanism of action.

L56 ANSWER 51 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:255350 HCAPLUS
DOCUMENT NUMBER: 118:255350
TITLE: antithrombic peptides and pseudopeptides
INVENTOR(S): Klein, Scott I.; **Molino, Bruce F.**; Czekaj, Mark; Gardner, Charles; Becker, Michael R.; Dener, Jeffrey M.; Pelletier, Jeffrey C.
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer International (Holdings) Inc., USA
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9217196	A1	19921015	WO 1992-US2637	19920330
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
CA 2107088	AA	19920929	CA 1992-2107088	19920330
AU 9220143	A1	19921102	AU 1992-20143	19920330
AU 673497	B2	19961114		
EP 577775	A1	19940112	EP 1992-912095	19920330
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 06506699	T2	19940728	JP 1992-511653	19920330
PRIORITY APPLN. INFO.:			US 1991-677006	A2 19910328
			WO 1992-US2637	A 19920330

OTHER SOURCE(S): MARPAT 118:255350
AB Title compds. (>150 compds.) were prepared Thus, polymer-bound Fmoc-Val-OH (Fmoc = 9-fluorenylmethoxycarbonyl) was treated with Fmoc-Asp(CMe3)-OH and Fmoc-Arg[SO2C6H(OMe)Me3-4,2,3,6]-OH followed by deprotection to give H-Arg-Asp-Val-OH (I). At 100μM I gave 49% inhibition of fibrinogen-mediated blood platelet aggregation.

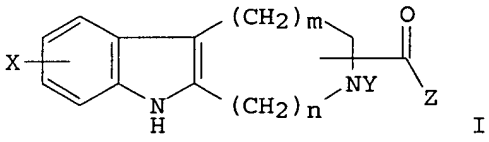
L56 ANSWER 52 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:256054 HCAPLUS
DOCUMENT NUMBER: 116:256054
TITLE: Preparation of peptide-linked 1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indoles and related compounds as inhibitors of cholecystokinin and gastrin
INVENTOR(S): **Molino, Bruce F.**; Darkes, Paul R.; Ewing, William R.
PATENT ASSIGNEE(S): Rorer International (Holdings), Inc., USA
SOURCE: PCT Int. Appl., 94 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9200295	A1	19920109	WO 1991-US4236	19910613
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
US 5162336	A	19921110	US 1990-573514	19900824
CA 2068887	AA	19911222	CA 1991-2068887	19910613
AU 9186116	A1	19920123	AU 1991-86116	19910613
AU 640277	B2	19930819		
EP 491943	A1	19920701	EP 1991-916717	19910613
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				

PRIORITY APPLN. INFO.: US 1990-542495 A 19900621
US 1990-573514 A2 19900824
WO 1991-US4236 A 19910613

OTHER SOURCE(S): MARPAT 116:256054
GI



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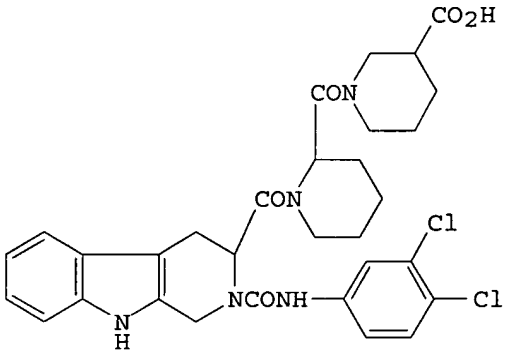

II

AB Title compds. [I; X = aryl; Y = H, alkyl, (substituted) aralkyl, acyl, aroyl, heterocyclylcarbonyl, carbamoyl, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl; Z = (substituted) N-containing heterocyclyl, amino, amino acid residue, peptide residue, etc.; m = 0-3; n = 0-4], were prepared Thus, (3R)-2-tert-butoxycarbonyl-1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole-3-carboxylic acid in THF at -15° was treated with Et3N and N,N-bis[2-oxo-3-oxazolinyl]phosphorodiamidic chloride followed by stirring for 20 min. Benzyl N-(L-prolyl)nipecotate was added and the mixture was stirred overnight at ice temperature to give the amide, which was deprotected with CF3CO2H followed by acylation with 3,4-dichlorophenyl isocyanate and hydrogenolysis to give title compound II. II bound to CCk-A, CCK-B, and gastrin receptors with IC50's of 10, 0.111, and 0.026 μM, resp.

L56 ANSWER 53 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:214925 HCAPLUS
DOCUMENT NUMBER: 116:214925
TITLE: Preparation of (guanidinobenzoyl)dipeptides and related compounds as antithrombotics
INVENTOR(S): Klein, Scott I.; **Molino, Bruce F.**
PATENT ASSIGNEE(S): Rorer Pharmaceutical Corp., USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5086069	A	19920204	US 1990-475043	19900205
WO 9218117	A1	19921029	WO 1991-US2471	19910411
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
AU 9180896	A1	19921117	AU 1991-80896	19910411
AU 661659	B2	19950803		
EP 584066	A1	19940302	EP 1991-910671	19910411
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 08503920	T2	19960430	JP 1991-510398	19910411
PRIORITY APPLN. INFO.:			US 1990-475043 A2	19900205
			WO 1991-US2471 A	19910411

OTHER SOURCE(S): MARPAT 116:214925
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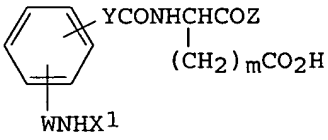


I

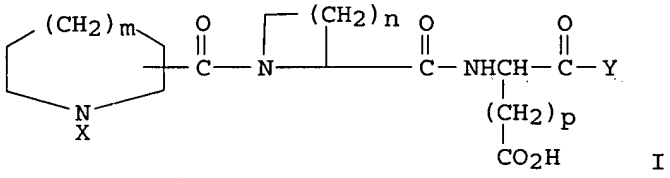
AB Title compds. [I; Y = (CH2)n, CH:CH, XCH2; X not defined; Z = NR1R2, OR1; W = (CH2)n CH:CH(CH2)p; R1, R2 = alkyl, aryl, aralkyl, allyl; m = 1-3; n = 0-6; p = 0-4; X1 = H, amidino], were prepared Thus, L-valine p-alkoxybenzyl alc. resin ester was coupled with N-(9-fluorenylmethoxycarbonyl)aspartic acid β-tert-Bu ester; the product was deprotected with piperidine in DMF followed by condensation with 3-(2-guanidinoethyl)benzoic acid hydrochloride (preparation given) and resin cleavage with CF3CO2H to give N-(3-(2-guanidinoethyl)benzoyl]aspartylvaline. N-(3-Guanidinomethylbenzoyl)aspartylvaline, prepared similarly, inhibited 125I-fibrinogen binding to platelets with IC50 = 0.25 μM.

L56 ANSWER 54 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1992:152412 HCAPLUS
DOCUMENT NUMBER: 116:152412
TITLE: Preparation of anti-thrombotic peptide and pseudopeptide derivatives
INVENTOR(S): Klein, Scott I.; **Molino, Bruce F.**
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals, Inc., USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5064814	A	19911112	US 1990-505286	19900405
US 5328900	A	19940712	US 1992-961216	19921015
PRIORITY APPLN. INFO.:			US 1990-505286 A2	19900405
			US 1991-724675 B1	19910702

OTHER SOURCE(S): MARPAT 116:152412
GI



I

AB The title compds. [I; X = H, amidino, COR1; R1 = alkyl, aryl, aralkyl; Y = OR2, NR2R3, naturally occurring L-amino acid residue; R2, R3 = H, alkyl, aryl, aralkyl, allyl; m = 0, 1, 2; n = 0, 1-4 integer; p = 0, 1-3 integer] and their pharmaceutically acceptable salts were prepared L-Aspartyl-β-tert-Bu ester-L-valine p-alkoxy benzyl resin ester (preparation given) was acylated with (S)-N-(9-fluorenylmethoxycarbonyl)azetidinyl-2-carboxylic acid (preparation given), the resulting (S)-N-(9-fluorenylmethoxycarbonyl)azetidinyl-2-carbonyl-L-aspartyl-β-tert-Bu ester-L-valine p-alkoxy benzyl resin ester deprotected and then condensed with N-tert-butoxycarbonyl-4-piperidinecarboxylic acid (preparation given), and the resulting resin-bound peptide deprotected and cleaved from the resin by means of CF3CO2H to give N-[2(S)-1-(piperidin-4-ylcarbonyl)azetidin-s-yl]-L-aspartyl-L-valine. This had an IC50 of 29.6 μM against fibrinogen-mediated platelet aggregation in an in vitro test.

L56 ANSWER 55 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:623777 HCAPLUS
DOCUMENT NUMBER: 115:223777
TITLE: Novel CCK-4 analogs with selectivity for gastrin receptors
AUTHOR(S): Ewing, W. Richard; **Molino, Bruce F.**; Pendley, Charles; Darkes, Paul R.; Kosmider, Benidict J.
CORPORATE SOURCE: Cent. Res., Rhone-Poulenc Rorer, King of Prussia, PA, 19406, USA
SOURCE: Pept. 1990, Proc. Eur. Pept. Symp., 21st (1991), Meeting Date 1990, 700-1. Editor(s): Giralt, Ernest; Andreu, David. ESCOM Sci. Publ.: Leiden, Neth. CODEN: 57HNAI
DOCUMENT TYPE: Conference
LANGUAGE: English
AB The tetrahydro-β-carboline replacement for the indole portion of Trp yielded compds. selective for gastrin receptors over cholecystokinin-A receptors.

L56 ANSWER 56 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:598524 HCAPLUS
DOCUMENT NUMBER: 115:198524

TITLE: Anti-thrombotic peptides and pseudopeptides for prophylaxis or treatment of abnormal thrombus formation
INVENTOR(S): Klein, Scott I.; **Molino, Bruce F.**; Czekaj, Mark; Gardner, Charles; Pelletier, Jeffrey C.
PATENT ASSIGNEE(S): Rorer International (Overseas), Inc., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9104746	A1	19910418	WO 1990-US5448	19900925
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
US 4952562	A	19900828	US 1989-415006	19890929
AU 9065391	A1	19910428	AU 1990-65391	19900925
AU 646411	B2	19940224		
EP 494248	A1	19920715	EP 1990-915350	19900925
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 05500954	T2	19930225	JP 1990-514349	19900925

PRIORITY APPLN. INFO.: US 1989-415006 A2 19890929
US 1990-534385 A 19900607
WO 1990-US5448 A 19900925
OTHER SOURCE(S): MARPAT 115:198524
AB The invention relates to novel peptides and pseudopeptides and pharmaceutical compns. containing them that inhibit blood platelet aggregation and that are useful for the prophylaxis or treatment of abnormal thrombus formation. Thus, L-ornithylglycyl-L-aspartylvaline (I) was prepared starting from L-valine tert-butyl ester via L-aspartyl-β-tert-butyl ester-L-valine α-tert-butyl ester, glycyl-L-aspartyl-β-tert-butyl ester-L-valine α-tert-butyl ester, N-α-tert-butyloxycarbonyl-N-5-benzyloxycarbonyl-L-ornithylglycyl-L-aspartyl-β-tert-butyl ester-L-valine α-tert-butyl ester, and N-α-tertbutyloxycarbonyl-L-ornithylglycyl-L-aspartyl-β-tert-butyl ester-L-valine tert-butyl ester. In vitro tests indicated that the IC50 value of I for inhibition of fibrinogen-mediated platelet aggregation was 15 μM. At 100 μM I, 80% inhibition was noted.

L56 ANSWER 57 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:598034 HCAPLUS
DOCUMENT NUMBER: 115:198034
TITLE: Novel RGD analogs as antithrombotic agents
AUTHOR(S): Klein, Scott I.; **Molino, Bruce F.**; Chu, Valeria; Ruggeri, Zaverio; Czekaj, Mark; Gardner, Charles J.; Newman, Jack; Barrett, John A.
CORPORATE SOURCE: Rhone-Poulenc Rorer Cent. Res., King of Prussia, PA, 19453, USA
SOURCE: Pept. 1990, Proc. Eur. Pept. Symp., 21st (1991), Meeting Date 1990, 374-5. Editor(s): Giralt, Ernest; Andreu, David. ESCOM Sci. Publ.: Leiden, Neth.
CODEN: 57HNAI
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A symposium report with 4 refs.

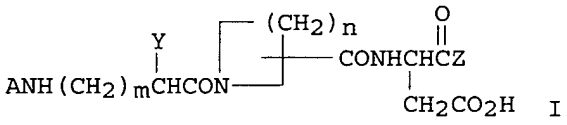
L56 ANSWER 58 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:583966 HCAPLUS
DOCUMENT NUMBER: 115:183966
TITLE: Antithrombotic peptides and pseudopeptides
INVENTOR(S): Klein, Scott I.; **Molino, Bruce F.**
PATENT ASSIGNEE(S): Rorer International (Overseas), Inc., USA
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9107976	A1	19910613	WO 1990-US6935	19901128
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
US 5053392	A	19911001	US 1989-444484	19891201
AU 9168900	A1	19910626	AU 1991-68900	19901128
AU 636426	B2	19930429		
EP 502926	A1	19920916	EP 1991-900107	19901128
EP 502926	B1	19960313		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05504762	T2	19930722	JP 1991-500883	19901128
AT 135367	E	19960315	AT 1991-900107	19901128

PRIORITY APPLN. INFO.: US 1989-444484 A1 19891201
WO 1990-US6935 A 19901128

OTHER SOURCE(S): MARPAT 115:183966
GI



I

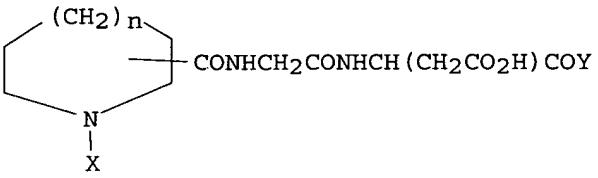
AB The title peptides (I; X = H, amidino, RCO; Y = H, NH2, RCONH; Z = NR1R2, OR1, naturally occurring L-amino acid residue; R = alkyl, aryl, aralkyl; R1, R2 = H, alkyl, aryl, aralkyl, allyl; m = 1-5; n = 0-4), which inhibit platelet aggregation and thrombus formation and useful for treatment of thrombogenic diseases, e.g. myocardial infarction and stroke, are prepared Thus, N-(5-guanidinopentanoyl)azetidine-2(S)-carboxyl-L-aspartyl-L-valine was prepared by the solid phase method and in vitro inhibited fibrinogen-mediated human platelet aggregation with IC50 of 1.2 μM. Addnl. 4 I were prepared

L56 ANSWER 59 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:583963 HCAPLUS
DOCUMENT NUMBER: 115:183963
TITLE: Preparation of tripeptide derivatives as antithrombotics
INVENTOR(S): Klein, Scott I.; **Molino, Bruce F.**; Czekaj, Mark; Gardner, Charles J.
PATENT ASSIGNEE(S): Rorer International (Holdings), Inc., USA
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9105562	A1	19910502	WO 1990-US5367	19900920
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
US 5051405	A	19910924	US 1989-419305	19891010
AU 9168837	A1	19910516	AU 1991-68837	19900920
PRIORITY APPLN. INFO.:			US 1989-419305 A	19891010
			WO 1990-US5367 A	19900920

OTHER SOURCE(S): MARPAT 115:183963
GI



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AB Tripeptide derivs. I (X = H, C(:NH)NH2, COR; Y = OH, OR1, L-amino acid residue such as Val-OH, Ser-OH, Gly-OH, etc.; R = alkyl, aryl, aralkyl; R1 = alkyl, aryl, aralkyl, allyl; n = 0-2) were prepared For example, title compound I (X = (C:NH)NH2, Y = Val-OH, n = 1) (II) was prepared via solid phase methods starting with resin-bound valine and subsequent coupling with Fmoc-Asp(OCMe3)-OH, Fmoc-Gly-OH, and N-amidino-4-piperidinecarboxylic acid hydrochloride (preparation given), followed by resin cleavage and deprotection. II at 100 μM showed 92% inhibition of fibrinogen mediated blood platelet aggregation.

L56 ANSWER 60 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:24611 HCAPLUS
DOCUMENT NUMBER: 114:24611
TITLE: Preparation of anti-thrombotic peptides and pseudopeptides
INVENTOR(S): Klein, Scott I.; **Molino, Bruce F.**; Czekaj, Mark; Gardner, Charles J.; Pelletier, Jeffrey C.
PATENT ASSIGNEE(S): Rorer Pharmaceutical Corp., USA
SOURCE: U.S., 9 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4952562	A	19900828	US 1989-415006	19890929
CA 2066047	AA	19910330	CA 1990-2066047	19900925
WO 9104746	A1	19910418	WO 1990-US5448	19900925
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
AU 9065391	A1	19910428	AU 1990-65391	19900925
AU 646411	B2	19940224		
EP 494248	A1	19920715	EP 1990-915350	19900925

R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE

JP 05500954	T2	19930225	JP 1990-514349	19900925
US 5332726	A	19940726	US 1992-859779	19920330
PRIORITY APPLN. INFO.:			US 1989-415006 A	19890929
			US 1990-460777 B2	19900104
			US 1990-534385 A	19900607
			WO 1990-US5448 A	19900925
			US 1991-677006 B2	19910328

OTHER SOURCE(S): CASREACT 114:24611; MARPAT 114:24611

AB XCH[(CH2)mNR1Y]ACH2BCH(CH2CO2H)(DCHECO2R2) (X = H, NR1R2; Y = H, alkyl, cycloalkyl, aralkyl, COR2; A, B, D = CONR2; E = H, Me, CHMe2; R1, R2 = H, alkyl; m = 2-8; when X = NH2, then m = 3, E = CHMe2, and ≥1 of A, B, D ≠ CONH), were prepared Thus, H-Arg-Gly-Asp-NHCH2CHMe2, prepared using fluorenylmethyloxycarbonyl-protected amino acids in the solution phase process, inhibited fibrinogen-mediated platelet aggregation with an IC50 of 3.6 μM.

L56 ANSWER 61 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1990:96275 HCAPLUS
DOCUMENT NUMBER: 112:96275
TITLE: Endothelium-dependent vascular responses: effect of hypertension and **cyclosporin** A
AUTHOR(S): Luescher, T. F.; **Yang, Z.**; Diederich, D.; Buehler, F. R.
CORPORATE SOURCE: Dep. Med., Univ. Hosp., Basel, Switz.
SOURCE: Zeitschrift fuer Kardiologie (1989), 78(Suppl. 6), 132-6
CODEN: ZKRDAX; ISSN: 0300-5860
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 39 refs. Through the release of endothelium-derived relaxing and contracting factors, the endothelium can profoundly affect local vascular tone. In hypertension and during chronic **cyclosporin** A therapy, morphol. changes of the endothelium develop. This review summarizes functional alterations of the endothelium under these conditions.

L56 ANSWER 62 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1989:173247 HCAPLUS
DOCUMENT NUMBER: 110:173247
TITLE: Preparation of heteroarene-fused diazacycloalkanones as cardiotonics
INVENTOR(S): Spada, Alfred P.; Campbell, Henry F.; Kuhla, Donald E.; Studt, William L.; Faith, William C.; **Molino, Bruce F.**
PATENT ASSIGNEE(S): Rorer International (Overseas), Inc., USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8803025	A1	19880505	WO 1987-US2879	19871027
W: AU, JP				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4859672	A	19890822	US 1986-925008	19861029
AU 8782327	A1	19880525	AU 1987-82327	19871027

EP 333727	A1	19890927	EP 1987-907490		19871027
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
JP 02500518	T2	19900222	JP 1987-506948		19871027
US 5002944	A	19910326	US 1989-350366		19890511
PRIORITY APPLN. INFO.:			US 1986-925008	A	19861029
			WO 1987-US2879	A	19871027

OTHER SOURCE(S): CASREACT 110:173247; MARPAT 110:173247

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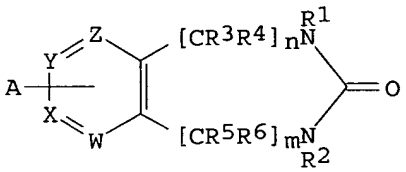

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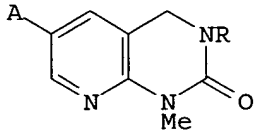

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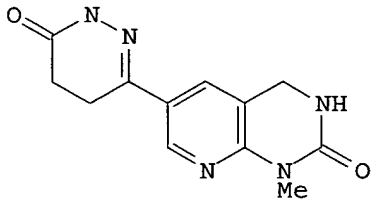

III

AB The title compds. [I; A = (un)substituted 2-pyridon-5-yl, 3-pyridazon-6-yl, 4-pyrimidon-6-yl, pyrimidine-2,4-dion-6-yl; 1 or 2 of W, X, Y, Z = N, the others = CR7, CR8, CR9; R1-R9 = H, alkyl, aryl, aralkyl; R7-R9 may addnl. bond with A; R3R4, R5R6 = O; m, n = 0,1] were prepared as cardiotonics (no data). 3-(Aminomethyl)-2-(methylamino)pyridine (preparation given) was refluxed 6 h with 1,1'-carbonyldiimidazole to give pyridopyrimidinone II (A = R = H) which was converted in 4 steps to II (A = Me3Sn, R = Ac). To latter was converted to II (A = COCH2CH2CO2Me, R = Ac) which was refluxed 8h with N2H4.H2O in EtOH to give title compound III.

L56 ANSWER 63 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	1989:173107 HCAPLUS
DOCUMENT NUMBER:	110:173107
TITLE:	6-(6-Alkylpyridone)carbostyril compounds and their use as inotropics
INVENTOR(S):	Campbell, Henry F.; Kuhla, Donald E.; **Molino, Bruce F.**; Studt, William L.
PATENT ASSIGNEE(S):	Rorer International (Overseas), Inc., USA
SOURCE:	PCT Int. Appl., 27 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8800188	A1	19880114	WO 1987-US1489	19870618
W: AU, JP, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4785005	A	19881115	US 1986-878123	19860625
AU 8776494	A1	19880129	AU 1987-76494	19870618
EP 311634	A1	19890419	EP 1987-904350	19870618

R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE

JP 01503456	T2	19891122	JP 1987-503968	19870618
PRIORITY APPLN. INFO.:			US 1986-878123	A2 19860625
			WO 1987-US1489	A 19870618

OTHER SOURCE(S): MARPAT 110:173107

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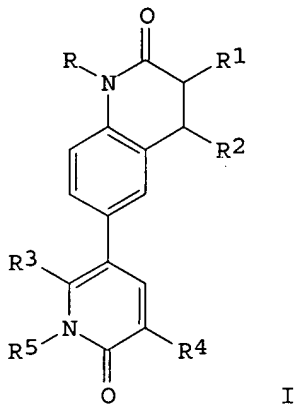

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AB Title compds. I (R-R3, R5 = H, alkyl; R4 = alkyl, alkoxyalkyl, hydroxyalkyl, cyano, carbamoyl, alkylcarbamoyl, CHO, alkyleneamino, NH2, halo) or their salts, useful as pos. inotropics, are prepared 6-(2-Bromopropionyl-3,4-dihydrocarbostyril was treated with KOAc and HOAc at reflux for 5 h to give the acetoxy derivative, which was reduced with NaBH4 in diglyme to give 6-(2-acetoxy-1-hydroxypropyl)-3,4-dihydrocarbostyril. The latter compound was dehydrated and hydrolyzed to 6-(2-oxopropyl)-3,4-dihydrocarbostyril, which was condensed with Me2NCH(OMe)2 to give 6-[1-(dimethylamino)-3-oxo-1-buten-2-yl]-3,4-dihydrocarbostyril. This compound was treated with 2-cyanoacetamide and NaH in DMF to give I (R-R2 = R5 = H, R3 = Me, R4 = cyano) (II). In the ganglionic-β blocked dog test, II at 30 μg/kg i.v. increased the contractile force by 97%, heart rate by 17%, and aortic blood flow by 51% with no change in arterial blood pressure. In contrast, milrinone (a known inotropic) at 100 μg increased contractile force by 111%, heart rate 19%, and aortic blood flow only transiently, while decreasing arterial blood pressure by 32%.

L56 ANSWER 64 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	1989:75899 HCAPLUS
DOCUMENT NUMBER:	110:75899
TITLE:	Synthetic and mechanistic studies based on pyrolysis products
AUTHOR(S):	Fraser-Reid, B.; Cusmano, John; Lowe, Derek; **Molino, Bruce**; Mootoo, David; Underwood, Russell; Farrell, Thomas; Khadem, John
CORPORATE SOURCE:	Paul M. Gross Chem. Lab., Duke Univ., Durham, NC, 27706, USA
SOURCE:	F.E.C.S. Int. Conf. Chem. Biotechnol. Biol. Act. Nat. Prod., [Proc.], 3rd (1987), Meeting Date 1985, Volume 1, 180-94. VCH: Weinheim, Fed. Rep. Ger. CODEN: 56IAAB
DOCUMENT TYPE:	Conference

LANGUAGE: English
AB A conference report on synthetic and mechanistic studies based on the pyrolysis products of the title polysaccharides.

L56 ANSWER 65 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:493054 HCAPLUS
DOCUMENT NUMBER: 109:93054
TITLE: Preparation of pyridonylbenzazinones and analogs as cardiotonics
INVENTOR(S): **Molino, Bruce F.**; Campbell, Henry F.; Kuhla, Donald E.; Studt, William L.
PATENT ASSIGNEE(S): Rorer International (Overseas), Inc., USA
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8801508	A1	19880310	WO 1987-US2007	19870813
W: AU, JP, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4764512	A	19880816	US 1986-900868	19860827
AU 8780303	A1	19880324	AU 1987-80303	19870813
EP 323479	A1	19890712	EP 1987-906236	19870813
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 02501302	T2	19900510	JP 1987-505653	19870813
PRIORITY APPLN. INFO.:			US 1986-900868	A2 19860827
			WO 1987-US2007	A 19870813

OTHER SOURCE(S): CASREACT 109:93054; MARPAT 109:93054
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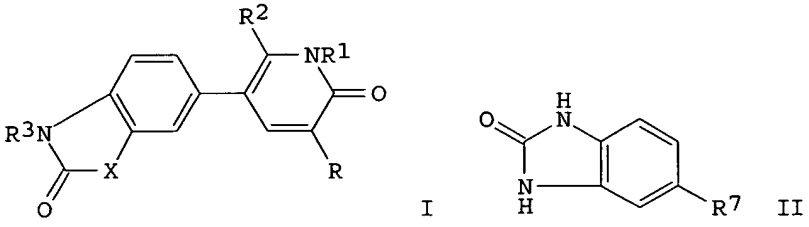

AB The title compds. [I; R = H, halo, cyano, NH2, H2NCO, alkyl, etc.; X = (CR4R5)aNR6(CR4R5)b; R1-R3, R5 = H, alkyl; R4, R6 = R1, aralkyl; a,b = 0-2; a + b = 0-2] were prepared as cardiotonics (no data). Dihydrobenzimidazole II (R2 = MeCHBrCO) (preparation given) was stirred 4 h with NaBH4 in MeOH containing NaOH to give II [R7 = MeOCHMeCH(OH)] which was refluxed 48 h in EtOAc with repeated addns. of 4-MeC6H4SO3H to give II (R7 = MeCOCH2). The latter was heated at 70° for 22 h with (MeO)2HCNMe2 and pyridine to give II (R7 = Me2NCH:CCOMe) which was added to H2NCOCH2CN in DMF previously treated with NaH and the mixture stirred 24 h to give I (R = cyano, R1 = R3 = H, R2 = Me, X = NH).

L56 ANSWER 66 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:204910 HCAPLUS
DOCUMENT NUMBER: 108:204910

TITLE: Stereoselectivity in the hydroboration of C4-C-methylene groups
AUTHOR(S): **Molino, Bruce F.**; Cusmano, John; Mootoo, David R.; Faghih, Ramine; Fraser-Reid, Bert
CORPORATE SOURCE: Dep. Chem., Duke Univ., Durham, NC, 27706, USA
SOURCE: Journal of Carbohydrate Chemistry (1987), 6(3), 479-93
CODEN: JCACDM; ISSN: 0732-8303
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 108:204910
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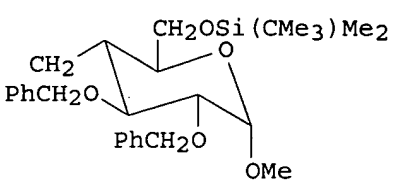

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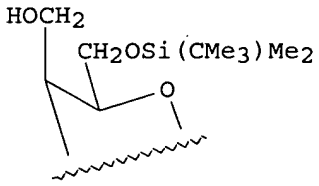

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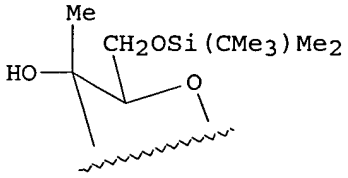


III

AB Conditions for the hydroxylation of an exocyclic methylene group at C-4 of a pyranoside ring via hydroboration were examined with a view to determining the optimum procedure for obtaining the axially-oriented C(4)-CH2OH group. The regio- and stereochem. outcome of the reactions depend not only on the hydroborating reagent used, but, to a surprising degree, on the nature of the protecting group at the remote C(6)-OH. Silyl ethers are preferred because the only byproduct formed is the tertiary alc., which can be recycled through dehydration to the starting alkene with SOCl2. Thus, C-methylene hexopyranoside I was treated with BH3 in THF and then with aqueous NaOH and H2O2 to give 40% hydroxymethyl derivative II and 25% alc. III.

L56 ANSWER 67 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:56472 HCAPLUS
DOCUMENT NUMBER: 108:56472
TITLE: Pyranosidic homologation. VII. Controlled formation of dipyranoside derivatives through carbon 6 and oxygen 4
AUTHOR(S): **Molino, Bruce Francis**; Fraser-Reid, Bert
CORPORATE SOURCE: Dep. Chem., Univ. Maryland, College Park, MD, 20742, USA
SOURCE: Canadian Journal of Chemistry (1987), 65(12), 2834-42
CODEN: CJCHAG; ISSN: 0008-4042
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 108:56472
GI

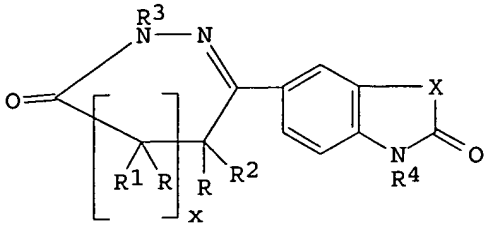
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB A procedure was developed for pyranosidic homologation of Me α-D-glucopyranoside via C(4) and C(6). Reaction of the aldehyde group of hexodialdopyranoside I with the Wittig-Bestmann reagent, Ph3P:CHCH(OEt)2, gave an E/Z mixture of acetals, II, which cyclized under the specific catalysis of pyridinium p-toluenesulfonate and in the presence of alcs. to give anomerically pure olefinic bipyranosides, III [R = Me, PhCH2, 4-MeOC6H4CH2, 3,4-(MeO)2C6H3CH2]. A general procedure for epoxidn. of the latter involved OsO4 hydroxylation, followed by reaction with phosgene iminium chloride (Viehe's salt) to give chlorocarbamates IV and V, which were then subjected to the action of sodium methoxide. This allowed for the formation of a single series of diastereomeric epoxides, VI, and controlled cleavage of VI with nucleophiles then followed well-established precedents. Selective access to the "ends" of VI [R = 4-MeOC6H4CH2, 3,4-(MeO)2C6H3CH2] were obtained by oxidative removal of the activated benzyl glycosides with DDQ.

L56 ANSWER 68 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:6037 HCAPLUS
DOCUMENT NUMBER: 108:6037
TITLE: Preparation of benzodiazinone-pyridazinones and hydroxypyrazole compounds as cardiotonics
INVENTOR(S): Kuhla, Donald Ernest; Campbell, Henry Flud; Studt, William Lyon; Faith, William Cass; **Molino, Bruce Francis**
PATENT ASSIGNEE(S): Rorer International (Overseas), Inc., USA
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8703201	A1	19870604	WO 1986-US2497	19861120
W: AU, JP, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4725686	A	19880216	US 1985-800986	19851122
AU 8767385	A1	19870701	AU 1987-67385	19861120
AU 600249	B2	19900809		
EP 247177	A1	19871202	EP 1987-900392	19861120
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 63502030	T2	19880811	JP 1987-500197	19861120
CA 1276145	A1	19901113	CA 1986-523546	19861121
US 4785101	A	19881115	US 1987-63481	19870617
US 4868300	A	19890919	US 1987-102083	19870721
US 4906630	A	19900306	US 1988-255664	19881011
PRIORITY APPLN. INFO.:			US 1985-800986	A2 19851122
			WO 1986-US2497	A 19861120
			US 1987-63481	A3 19870617

OTHER SOURCE(S): CASREACT 108:6037; MARPAT 108:6037
GI



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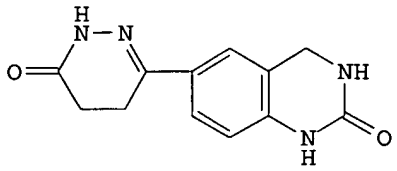

II

AB The title compds. [I; X = (CR5R6)aNR7(CR5R6)b; R, R2-R7 = H, alkyl, aralkyl; R2 = (un)substituted C1-3 alkyl; R2,R52, R6R7 = bond; R5R6 = C2-5 alkylene; a + b = 0-2; x = 0, 1] and their pharmaceutically acceptable salts were prepared as pos. inotropic agents, useful in treating congestive heart failure (no data). 3,4-Dihydro-2(1H)-quinazolinone underwent Friedel-Crafts acylation by refluxing in CS2 with MeO2CCH2CH2COCl and AlCl3 to give 6-(3-carboxypropionyl)-3,4-dihydro-2(1H)-quinazolinone. This was refluxed in EtOH with N2H4.H2O to give (oxopyridazinyl)quinazolinone II.

L56 ANSWER 69 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:598793 HCAPLUS
DOCUMENT NUMBER: 107:198793
TITLE: Tripyranoside precursors for ansamycins. Pyranosidic homologation. 6
AUTHOR(S): Fraser-Reid, Bert; **Molino, Bruce F.**; Magdzinski, Leon; Mootoo, David R.
CORPORATE SOURCE: Paul M. Gross Chem. Lab., Duke Univ., Durham, NC, 27706, USA
SOURCE: Journal of Organic Chemistry (1987), 52(20), 4505-11
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 107:198793
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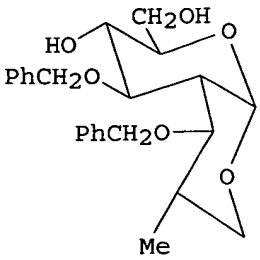

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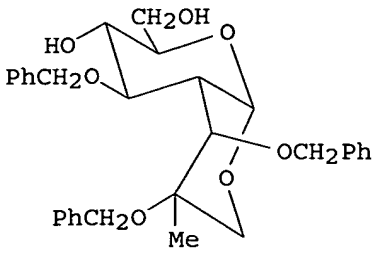

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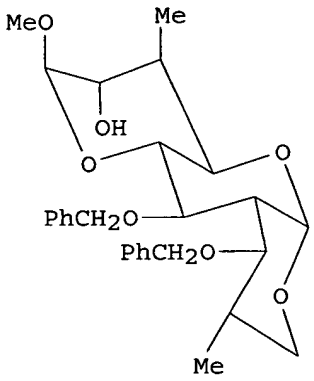

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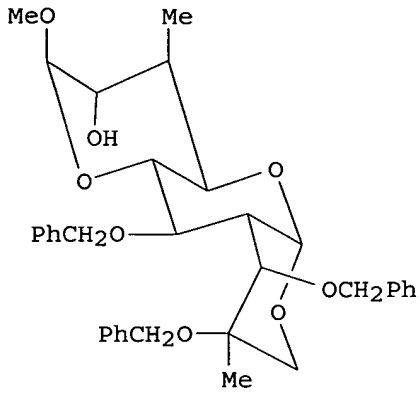

IV

AB The primary and secondary alcs. of the dipyranoses I and II were used as implements for elaborating the upper pyranoside rings of the tripyranoses III and IV, resp. III contains seven of the eight chiral centers of rifamycin S, while IV fixes seven of the nine chiral centers of streptovaricin A. For the synthetic procedures, the primary alc. was oxidized to an aldehyde, which was subjected to olefination with a phosphorane of the type PH3P:CHCH(OR)2. Treatment with pyridinium p-toluenesulfonate, specifically, in the presence of an alc. caused cyclization with the secondary alc., resulting in a hexenopyranoside, which was glycosidated in situ by the alc. The resulting hexenopyranoside was then epoxidized, by a new procedure that involved hydroxylation with OsO4 and treatment of the cis diol so formed with phosgene iminium chloride (Viehe's salt) to give a chloro carbamate, which then reacted with methoxide to give the desired epoxide. Opening of the ring with Me2Mg then completed the requirements for the upper ring.

L56 ANSWER 70 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:554621 HCAPLUS
DOCUMENT NUMBER: 107:154621
TITLE: Dipyranoside precursors for ansamycins. Pyranosidic homologation. 5
AUTHOR(S): Fraser-Reid, Bert; Magdzinski, Leon; **Molino, Bruce F.**; Mootoo, David R.
CORPORATE SOURCE: Paul M. Gross Chem. Lab., Duke Univ., Durham, NC, 27706, USA
SOURCE: Journal of Organic Chemistry (1987), 52(20), 4495-504
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 107:154621
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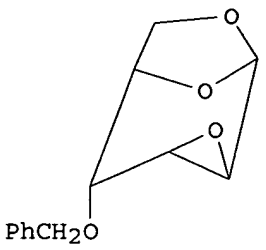

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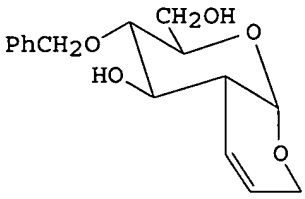

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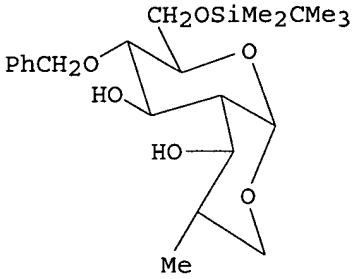

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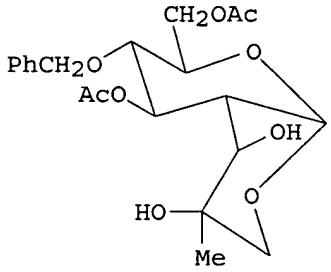


IV

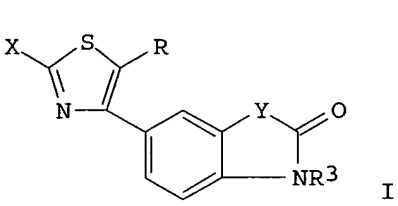
AB The process of pyranosidic homologation was applied to the readily obtainable dianhydro sugar I in the context of preparation of precursors for mols. containing multiple contiguous chiral centers (e.g., the ansa chains of rifamycin S and streptovaricin A). Two approaches for construction of the lower satellites were determined The first involved opening of the epoxide I with a carbanion derived from propargyl alc., followed by Lindlar reduction Treatment of the resulting allylic alc. with CF3CO2H lead to internal glycosidation; the cis-fused (i.e., α) bicyclic system II being highly favored. II on sequential silylation, epoxidn., epoxide ring cleavage with LiMe2C4, pyridinium chlorochromate oxidation, and LiAlH4 reduction gave III the precursor for rifamycin S. Also prepared from I was IV, required for streptovaricin A.

L56 ANSWER 71 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:496711 HCAPLUS
DOCUMENT NUMBER: 107:96711
TITLE: Preparation of hydroxy- and aminothiazolylbenzodiazinones as cardiotonic agents
INVENTOR(S): Kubla, Donald E.; Campbell, Henry F.; Studt, William L.; **Molino, Bruce F.**; Tucker, Thomas J.
PATENT ASSIGNEE(S): William H. Rorer, Inc., USA
SOURCE: U.S., 12 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4666913	A	19870519	US 1985-801071	19851122
WO 8703199	A1	19870604	WO 1986-US2496	19861120
W: AU, JP				

RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE					
AU 8767386	A1	19870701	AU 1987-67386		19861120
AU 582982	B2	19890413			
EP 247167	A1	19871202	EP 1987-900025		19861120
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
JP 63502031	T2	19880811	JP 1987-500198		19861120
PRIORITY APPLN. INFO.:			US 1985-801071	A	19851122
			WO 1986-US2496	A	19861120

OTHER SOURCE(S): CASREACT 107:96711; MARPAT 107:96711
GI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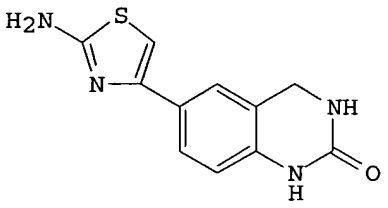
II

AB The title compds. [I; X = NR1R2, OH; Y = (CR4R5)aNR6(CR4R5)b; a, b = 0-2, a + b ≤ 2; R, R1, R2, R3, R4, R5, R6 = H, alkyl, aralkyl; adjacent R4 groups may be double bond; R4R5 may be (CH2)d; d = 2-5] are prepared as cardiotonic agents (no data). Friedel-Crafts acylation of 2.6 g 3,4-dihydro-2(1H)-quinazolinone by 6.2 g BrCH2COCl in refluxing CS2 with AlCl3 catalyst gave the crude 6-(bromoacetyl) derivative, which (3 g) underwent cyclocondensation with 0.9 g thiourea in refluxing EtOH to give (aminothiazolyl)quinazolinone derivative II.

L56 ANSWER 72 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	1987:440203 HCAPLUS
DOCUMENT NUMBER:	107:40203
TITLE:	A ready route from vicinal cis-diols to epoxides
AUTHOR(S):	Sunay, Ustun; Mootoo, David; **Molino, Bruce**; Fraser-Reid, Bert
CORPORATE SOURCE:	Paul M. Gross Chem. Lab., Duke Univ., Durham, NC, 27706, USA
SOURCE:	Tetrahedron Letters (1986), 27(39), 4697-700 CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE:	Journal
LANGUAGE:	English
OTHER SOURCE(S):	CASREACT 107:40203

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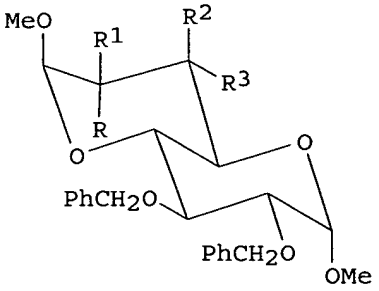
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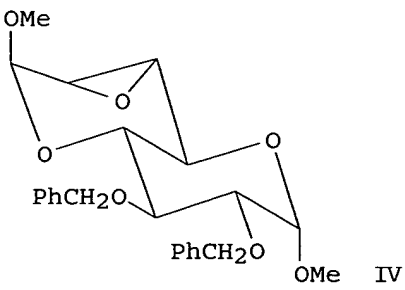
IV

AB A two-step procedure for converting a vicinal cis-diol into epoxides is described which involves the preparation of chlorocarbamate intermediate by the use of Me2R1+:CCl2 Cl-. For example, treatment of diol (I; R = R3 = OH, R1 = R2 = H) with Me2N+:CCl2Cl- in CH2Cl2 in the presence of Et3N at reflux gave chlorocarbamates [I; R = Me2NCO2, R1 = R3 = H, R2 = Cl (II); R = R2 = H, R1 = Cl, R3 = Me2NCO2 (III)] in 82 and 5% yield, resp. Treatment of II with NaOMe gave 70% epoxide IV. III did not react with NaOMe.

L56 ANSWER 73 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:626538 HCAPLUS
DOCUMENT NUMBER: 105:226538
TITLE: Bicyclic heteroaryl thiazole compounds and their cardiotonic uses
INVENTOR(S): Kuhla, Donald Ernest; Campbell, Henry Flud; Studt, William Lyon; **Molino, Bruce Francis**
PATENT ASSIGNEE(S): Rorer International (Overseas), Inc., USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 8603749	A1	19860703	WO 1985-US2522		19851218
W: AU, JP, US					
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE					
US 4721721	A	19880126	US 1984-683204		19841218
AU 8652388	A1	19860722	AU 1986-52388		19851218
EP 207140	A1	19870107	EP 1986-900535		19851218
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE					
JP 62501417	T2	19870611	JP 1986-500472		19851218
US 4818755	A	19890404	US 1986-897064		19860728
PRIORITY APPLN. INFO.:			US 1984-683204	A2	19841218
			CA 1985-497858	A	19851217
			WO 1985-US2522	A	19851218

OTHER SOURCE(S): CASREACT 105:226538; MARPAT 105:226538
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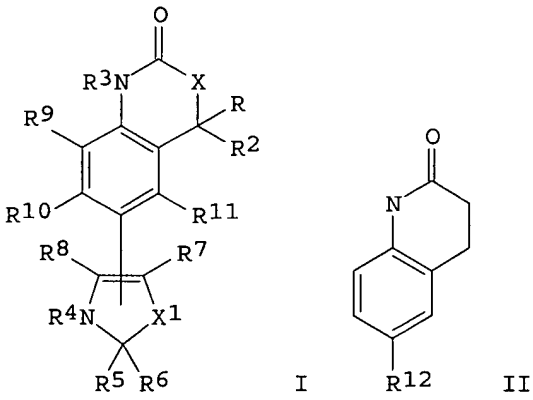


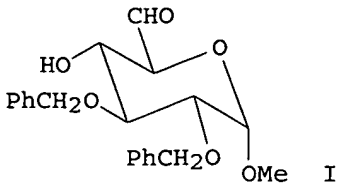
I

II

AB Title compds. I [X = bond, CR:CR, CRR1, CRR2CRR2; X1 = N, S; R, R3, R7, R8 = H, alkyl; R1 = H, alkyl, OH, amino, acetamido; R2 = H, alkyl; R1R2 = bond; RR2 = (CH2)2-5; R4R5 = bond; NR4CR5 = imidazo; R6 = H, (substituted) alkyl, aryl, amino, amidino, OH, N-containing heterocycle; R9-R11 = H, alkyl, alkoxy, OH, alkylthio, alkylsulfinyl, alkylsulfonyl], useful for the treatment of congestive heart disease (no data), were prepared Thus, PhNH2 reacted with ClCH2CH2COCl to give ClCH2CH2CONHPh, which cyclized in the presence of AlCl3 to give quinolinone II (R12 = H), which was treated with ClCH2COCl-AlCl3 to form II (R12 = COCH2Cl). This cyclized on reaction with H2NCSNH2 to give II (R12 = 2-aminothiazol-4-yl).

L56 ANSWER 74 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:149285 HCAPLUS
DOCUMENT NUMBER: 104:149285
TITLE: Pyranosidic homologation a carbohydrate approach to the synthesis of the ansa chains of streptovaricin A and rifamycin S
AUTHOR(S): **Molino, Bruce Francis**
CORPORATE SOURCE: Univ. Maryland, College Park, MD, USA
SOURCE: (1984) 233 pp. Avail.: Univ. Microfilms Int., Order No. DA8510266
From: Diss. Abstr. Int. B 1985, 46(3), 844
DOCUMENT TYPE: Dissertation
LANGUAGE: English
AB Unavailable

L56 ANSWER 75 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:175150 HCAPLUS
DOCUMENT NUMBER: 100:175150
TITLE: Pyranosidic homologation: Part I: Extending the carbohydrate template via C6 and C4
AUTHOR(S): **Molino, Bruce F.**; Magdzinski, Leon; Fraser-Reid, Bert
CORPORATE SOURCE: Dep. Chem., Univ. Maryland, College Park, MD, 20742, USA
SOURCE: Tetrahedron Letters (1983), 24(52), 5819-22
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 100:175150
GI



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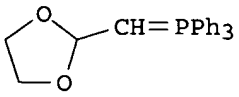
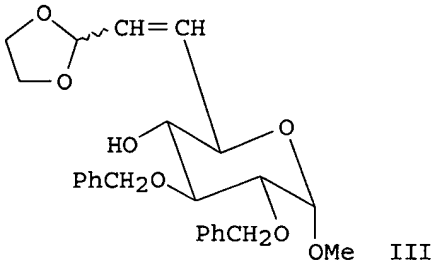


II



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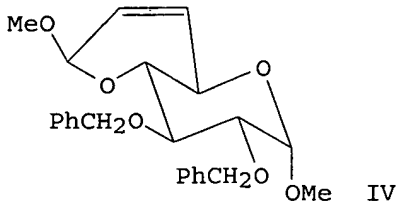

IV

AB The aldehyde I reacts with ylide (II) to give III as a 4:1 Z/E mixture which, upon methanolysis under catalysis by pyridinium p-toluenesulfonate, affords the bispyranoside IV as a single anomer.

L56 ANSWER 76 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:68612 HCAPLUS
DOCUMENT NUMBER: 100:68612
TITLE: New strategy for carbohydrate-based syntheses of multichiral arrays: pyranosidic homologation. 2
AUTHOR(S): Fraser-Reid, Bert; Magdzinski, Leon; **Molino, Bruce**
CORPORATE SOURCE: Chem. Dep., Univ. Maryland, College Park, MD, 20742, USA
SOURCE: Journal of the American Chemical Society (1984), 106(3), 731-4
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A process of pyranosidic homologation has been developed whereby ''satellite'' pyranosides are attached to the front and rear of a ''backbone'' pyranoside. The resulting manifold has capacity for eight contiguous chiral centers, two of which survive from the starting levoglucosan. The other six are introduced rationally and with complete stereo- and/or regioselectivity in each case, and configurational assignments are readily made by 200-MHz 1H NMR. The study is outlined with respect to a key intermediate for the ansa chain of rifamycin, but the general applicability to other pseudo higher carbon sugars, as well as their authentic counterparts, is clearly obvious.

L56 ANSWER 77 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1983:405905 HCAPLUS
DOCUMENT NUMBER: 99:5905
TITLE: Carbohydrate derivatives in the asymmetric synthesis of natural products
AUTHOR(S): Fraser-Reid, Bert; Magdzinski, Leon; **Molino, Bruce**
CORPORATE SOURCE: Chem. Dep., Univ. Maryland, College Park, MD, 20742, USA
SOURCE: Curr. Trends Org. Synth., Proc. Int. Conf., 4th (1983)

, Meeting Date 1982, 197-204. Editor(s): Nozaki, Hitosi. Pergamon: Oxford, UK.
CODEN: 49OPAS
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 30 refs.

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